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THESYNAPSE

THE MEDICAL PROFESSIONALS' NETWORK

- Negligence and Civil Liability in the Medical Profession
- Pitfalls in death certification
- Bioresorbable vascular scaffolds: the way forward?
- Meeting Maria Galea

Volume 14 Issue 06 ISSN number 2313-8084

Augmentin® ES

600 mg/42.9 mg/5 ml

Amoxicillin/Clavulanate Potassium

Powder for oral suspension

- ✓ Provides extended antibacterial coverage to include the most penicillin-resistant strains.[1]
- ✓ Recommended by leading Guidelines as first line treatment in AOM.[2,3]
- ✓ Most common adverse effects are diarrhoea, nausea, vomiting and mucocutaneous candidiasis.[4]
- ✓ Indicated for children <40 kg and older than 3 months; dosed at 90/6.4 mg/kg/day in 2 divided doses.[4]

Spreading infectious energy!

Mini Abridged Prescribing Information: *Please refer to full Summary of Product Characteristics (SPC) before prescribing.* **TRADE NAME:** Augmentin ES. **ACTIVE INGREDIENTS:** Amoxicillin (as trihydrate) and potassium clavulanate. **PRESENTATION:** 600 mg/42.9 mg/5 ml powder for oral suspension. Supplied in 100 ml glass bottle with a dosing spoon. **INDICATION:** treatment of acute otitis media and community acquired pneumonia infections in children aged at least 3 months and less than 40 kg body weight, caused or thought likely to be caused by penicillin-resistant *Streptococcus pneumoniae*. **POSOLOGY & ADMINISTRATION:** Oral use. Recommended dose is 90/6.4 mg/kg/day in two divided doses. To minimise potential gastrointestinal intolerance, administer at the start of a meal. **CONTRAINDICATIONS:** Hypersensitivity (and past history of) to the active substances, to any penicillins or to any of the excipients. **SPECIAL WARNINGS & PRECAUTIONS:** Before initiating therapy careful enquiry of previous hypersensitivity reactions to beta-lactams. Where an infection is proven to be due to an amoxicillin susceptible organism, a switch to an amoxicillin-only preparation should be considered. Convulsions may occur in patients receiving high doses or who have impaired renal function. Concomitant use of allopurinol increase likelihood of allergic skin reactions. Prolonged use may occasionally result in overgrowth of non-susceptible organisms. Contains aspartame (E951), a source of phenylalanine. The suspension also contains maltodextrin (glucose). **INTERACTIONS:** Penicillins may reduce the excretion of methotrexate causing a potential increase in toxicity. Concomitant use of probenecid is not recommended. If co-administration with oral anticoagulants is necessary, the prothrombin time or international normalised ratio should be carefully monitored with the addition or withdrawal of amoxicillin. Moreover, adjustments in the dose of oral anticoagulants may be necessary. Clinical monitoring should be performed during the combination with mycophenolate mofetil and shortly after antibiotic treatment. **PREGNANCY & LACTATION:** Use should be avoided unless considered essential by the physician. **UNDESIRABLE EFFECTS:** Very common (≥1/10): diarrhoea. Common (≥1/100, <1/10): mucocutaneous candidosis, nausea, abdominal pain. *Refer to SPC's for full list of undesirable effects*. **AUTHORISATION NUMBER:** AA 1051/00101. **MARKETING AUTHORISATION HOLDER:** GlaxoSmithKline Bulgaria EOOD. **LEGAL CATEGORY:** POM. **DATE OF PREPARATION:** July 2014. **In order to ensure that this product information reflects the most up-to-date clinical and post-marketing surveillance data, please always refer to the latest Summary of Product Characteristics (SPC) which is available from GlaxoSmithKline (Malta) Ltd (Tel: +356 21238131).** ***REPORTING ADVERSE EVENTS (AEs):*** **If you become aware of any AEs, medication errors and/or use during pregnancy in association with GSK products, please report the event promptly to:** GSK (Malta) Limited, 1, De la Cruz Avenue, Qormi QRM 2458, Malta (Tel: +356 21238131). **Alternatively, any suspected AEs and medication errors can also be reported via the national Adverse Drug Reactions (ADRs) reporting system:** Report forms can be downloaded from www.medicinesauthority.gov.mt/adrportal and posted to the Malta Medicines Authority, Post-licensing Directorate, 203, Level 3, Rue D'Argens, Gżira GŻR 1368, MALTA, or sent by email to postlicensing.medicinesauthority@gov.mt.

References:

1. Anthony R. White *et al*. Augmentin® amoxicillin/clavulanate) in the treatment of community-acquired respiratory tract infection: a review of the continuing development of an innovative antimicrobial agent Journal of Antimicrobial Chemotherapy (2004) 53, Suppl. S1, i3–i20.
2. Gilbert DN, *et al*. Sanford guide to Antimicrobial Therapy v.3.11 – last updated March 11, 2014. Sperryville; Antimicrobial Therapy, Inc. 2014.
3. Lieberthal AS *et al*. The Diagnosis and Management of Acute Otitis Media. Pediatrics. 2013; 131; e964 Epub 2013 Feb 25.
4. Augmentin ES Summary of Product Characteristics, May 2015.

Prepared: September 2015
Job No: MLT_GIB/AES/0001/15(2)

AVATAR CLINICIANS? TRY *JAZZ* FOR CHRISTMAS

Jazz is defined as a genre of music which originated during the late 19th and early 20th century. However in our case, the term Jazz is referring to a remote presence system for doctors, developed by the French company Gostai. In essence it may also be called an avatar system.

Jazz consists of a 3 foot robot possessing an articulated head mounted with an LCD screen, a docking station (for charging), as well as an Urbi open-source cross-platform software platform in C++. According to French surgeon Dr Alain Herard, Jazz has greatly facilitated his life. Like all surgeons, he needs to carry out operations, visit his patients and do the paperwork. Whilst Dr Herard is in his office carrying out his paperwork, he wears an over-the-head wireless headset and stands in front of a computer camera which is connected to Jazz through Wifi. On the other hand, Jazz visits his patients. Since the robot is fitted with camera, speakers and microphones, Dr Herard sees what Jazz sees, hears what Jazz hears and talks through Jazz to his patients via the speaker. More importantly, the patient gets to actually see the doctor through the 5 inch LCD screen and speak to him through the microphone.

One of the most distinguishing features of Jazz is the web-based remote control interface. The robot is driven by clicking with the mouse on the video feed. If one is driving the robot and the video shows a long corridor, one simply click at the end of the corridor and the robot will go there. In addition, since it possesses a built-in infrared camera and telemetric laser system, this €9000 robot can map its own surroundings and eventually patrol buildings fully autonomously.

Such technology may be the linchpin in the provision of medical care in remote rural areas of large countries, which may be disadvantaged because of the long travelling distances needed to access medical care. However, the use of this technology also has its relevance locally. Using an avatar system, visiting consultants who operate at Mater Dei hospital may 'visit' patients before actually arriving in Malta. Furthermore, imagine that at 2am a Consultant receives a phone call from a Resident Specialist at Mater Dei hospital, requesting his presence because of an emergency. As long as there is a computer connected to the internet, the Consultant can instantly be 'present' at the hospital through Jazz and interact with patients and medical staff.

Ian Ellul

Cover: The Central Hospital in Floriana was inaugurated in 1850 as a general hospital. Patients from the Valletta Civil Hospital were transferred there. The building, constructed in 1734, was previously used to house and teach poor girls. In 1954 it was converted into the Malta Police Force Headquarters.

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OUR COLLABORATORS

GMMS German-Maltese Medical Society · MMSA · MPSA · MADS

The magazine is distributed free of charge to all Maltese doctors, pharmacists & dentists, as well as students of the aforementioned professions, with a print run of 3500 copies.

Annual subscription rates outside Malta: Six issues €90 or equivalent, worldwide

A maintenance bronchodilator treatment for patients with COPD who are breathless

ANORO™ ELLIPTA™

umeclidinium/vilanterol

breathe...

Anoro® Ellipta® (umeclidinium bromide/vilanterol) Abridged Prescribing Information

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 on SPC how to report adverse reactions.

Kindly consult the full Summary of Product Characteristics (SmPC) before prescribing

Trade Name: Anoro® Ellipta® **Active Ingredients:** 55 micrograms umeclidinium bromide and 22 micrograms vilanterol (as trifenatate). **Pharmaceutical Form:** 55 micrograms/22 micrograms inhalation powder, pre-dispensed. **Indications:** Maintenance bronchodilator treatment to relieve symptoms in adult patients with Chronic Obstructive Pulmonary Disease (COPD). **Dosage and administration:** Inhalation only. One inhalation once daily of Anoro® Ellipta® at the same time of the day. **Contraindications:** Hypersensitivity to the active substances or to any of the excipients (lactose monohydrate and magnesium stearate). **Precautions:** Anoro® Ellipta® should not be used in patients with asthma. Treatment with Anoro® Ellipta® should be discontinued immediately in the event of paradoxical bronchospasm and alternative therapy initiated if necessary. Cardiovascular effects may be seen after the administration of muscarinic receptor antagonists and sympathomimetics therefore Anoro® Ellipta® should be used with caution in patients with severe cardiovascular disease. Anoro® Ellipta® should be used with caution in patients with urinary retention, narrow angle glaucoma, convulsive disorders, thyrotoxicosis, hypokalaemia, hyperglycaemia and severe hepatic impairment. No dosage adjustment is required in the elderly, in renal impairment or mild to moderate hepatic impairment. **Acute symptoms:** Anoro® Ellipta® is not indicated for acute episodes of bronchospasm. Warn patients to seek medical advice if use of short-acting inhaled bronchodilator increases. A re-evaluation of the patient and of the COPD treatment regimen should be undertaken. **Interactions with other medicinal products:** Interaction studies have only been performed in adults. Avoid beta- adrenergic blockers since this may weaken or antagonize the effect of $beta_2$-adrenergic agonists. Caution is advised when co-administering with strong CYP3A4 inhibitors (e.g. ketoconazole, clarithromycin, itraconazole, ritonavir, telithromycin). Anoro® Ellipta® should not be used in conjunction with other long-acting muscarinic antagonists, long-acting $beta_2$-adrenergic agonists or medicinal products containing either of these agents. Caution is advised with concomitant use with methylxanthine derivatives, steroids or non-potassium-sparing diuretics as it may potentiate possible hypokalaemic effect of $beta_2$-adrenergic agonists. **Fertility, pregnancy, and breast-feeding:** No available data. Balance risks against benefits. **Side effects:** Common: Urinary tract infection, sinusitis, nasopharyngitis, pharyngitis, upper respiratory tract infection, headache, cough, oropharyngeal pain, constipation and dry mouth. Uncommon: Atrial fibrillation, supraventricular tachycardia, rhythm idioventricular, tachycardia, supraventricular extrasystoles and rash. **Legal category:** POM. **Presentation:** Anoro® Ellipta®. 1 inhaler x 30 doses. Anoro® Ellipta® 55/22mcg. **Marketing authorisation (MA) nos:** 55/22mcg 1x30 doses [EU/1/14/898/002]; **MA holder:** Glaxo Group Ltd, 980 Great West Road, Brentford, Middlesex, TW8 9GS, UK. **Last date of revision:** October 2014. Anoro® and Ellipta® are registered trademarks of the GlaxoSmithKline group of companies. All rights reserved. Anoro® Ellipta® was developed in collaboration with Theravance, Inc.

In order to ensure that this product information reflects the most up-to-date clinical and post-marketing surveillance data, please always refer to the latest Summary of Product Characteristics (SPC) which is available from GlaxoSmithKline (Malta) Ltd (Tel: +356 21238131)

REPORTING ADVERSE EVENTS (AEs):

Malta & Gibraltar: **If you become aware of any AEs, medication errors and/or use during pregnancy in association with GSK products, please report the event promptly to:** GSK (Malta) Limited, 1, De la Cruz Avenue, Qormi QRM 2458, Malta (Tel: +356 21238131)

Malta: **alternatively, any suspected AEs and medication errors can also be reported via the national Adverse Drug Reactions (ADRs) reporting system:**

Report forms can be downloaded from www.medicinesauthority.gov.mt/adrportal and posted to the Malta Medicines Authority, Post-licensing Directorate, 203, Level 3, Rue D'Argens, Gżira GŻR 1368, MALTA, or sent by email to postlicensing.medicinesauthority@gov.mt

Gibraltar: **alternatively, any suspected AEs and medication errors can also be reported via the UK regulatory authority (MHRA):** https://yellowcard.mhra.gov.uk/

ANORO ELLIPTA was developed in collaboration with Theravance

Theravance

MLT_GIB/UCV/0004/15 Date of preparation: March 2014

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ISSUE GUIDE

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THESYNAPSE eLearning Videos

Content that matters
for the busy medical professional

This video is intended to give an overview of Medical Indemnity Insurance and is the first video of its kind on The Synapse. For this interview we invited Mr. Peter England from England Insurance Agency who has specialised in Medical Indemnity insurance since 2001. Since then Mr. England has negotiated various group schemes and has also given product presentations to various associations.

Following the enactment of the EU Healthcare directive in November 2013 Medical Indemnity insurance became obligatory. At that time healthcare professionals had the choice to take up Union membership or insurance. Following the recent market developments with the withdrawal of UK protection union memberships in Malta more and more doctors are seeking to transfer the indemnity risk to a new provider.

England Insurance Agency represents Mapfre Middlesea and also offers the MAM scheme, Paediatrics and GP group schemes amongst others. For further information and a no obligation meeting you may contact Mr. England on 9947 5752 or 21251015. Email peter@england.com.mt.

Visit www.thesynapse.net/videos for these and other interesting eLearning videos

Available on the App Store Google play

HEARD IN THE Grapevine

WHY ELEPHANTS DO NOT GET CANCER

In reality, < 5% of elephants suffer from cancer. However, this verges on the illogical since large-bodied animal cells should have divided more frequently than those of smaller size animal cells. Thus, random mutations which in turn predispose to cancer should also be more frequent. This is known as Peto's paradox, named after Sir Richard Peto, hailing from Oxford University, who described this lack of correlation in the 1970s. The main reason for this has now been attributed to the fact that elephants have 20 copies of TP53 which is a key tumour-fighting gene in their genome.1,2 In comparison, humans only have one copy.

References

1. Abegglen LM et al. Preliminary Communication. Potential Mechanisms for Cancer Resistance in Elephants and Comparative Cellular Response to DNA Damage in Humans. JAMA; 2015.
2. Sulak M. et al. TP53 copy number expansion correlates with the evolution of increased body size and an enhanced DNA damage response in elephants. Preprint at bioRxiv; 2015.

astellas

Prescribing Information Presentation: Betmiga™ prolonged release tablets containing 25 mgor 50 mg mirabegron. **Indication:** Symptomatic treatment of urgency, increased micturition frequency and/or urgency incontinence as may occur in adult patients with overactive bladder (OAB) syndrome. **Dosage:** Adults (including the elderly): Recommended dose: 50 mg once daily. Children and adolescents: Should not be used. **Contraindications:** Hypersensitivity to active substance or any of the excipients. **Warnings and Precautions:** Should not be used in patients with end stage renal disease, severe hepatic impairment and severe uncontrolled hypertension. Not recommended in patients with severe renal impairment and moderate hepatic impairment concomitantly receiving strong CYP3A inhibitors. Dose adjustment to 25 mg is recommended in patients with moderate renal and mild hepatic impairment receiving strong CYP3A inhibitor concomitantly. Caution in patients with a known history of QT prolongation or in patients taking medicines known to prolong the QT interval. Not recommended during pregnancy and in women of childbearing potential not using contraception. Not recommended during breastfeeding. **Interactions:** Clinically relevant drug interactions between Betmiga™ and medicinal products that inhibit, induce or are a substrate for one of the CYP isozymes or transporters are not expected, except for inhibitory effect on the metabolism of CYP2D6 substrates. Betmiga™ is a moderate and time-dependant inhibitor of CYP2D6 and weak inhibitor of CYP3A. No dose adjustment needed when administered with CYP2D6 inhibitors or CYP2D6 poor metabolisers. Caution if co-administered with medicines with a narrow therapeutic index and significantly metabolised by CYP2D6. When initiating in combination with digoxin the lowest dose for digoxin should be prescribed and serum digoxin should be monitored. **Adverse Effects:** Urinary tract infection, tachycardia, palpitation, atrial fibrillation, blood pressure increase, leukocytoclastic vasculitis. Prescribers should consult the Summary of Product Characteristics in relation to other side effects. **Pack and Prices:** Country specific. **Legal Category:** POM. Product Licence Number: Betmiga™ 25 mg EU/1/12/809/003; Betmiga™ 50 mg EU/1/12/809/010. **Date of Preparation:** November 2012 **Further information available from:** Astellas Pharma Europe B.V. P.O. Box 344, 2300 AH Leiden, The Netherlands. Betmiga™ is a Registered Trademark. For full prescribing information please refer to the Summary of Product Characteristics. 20140312-UR-BTMA-08

Adverse events should be reported. Report adverse events to E.J. Busuttil Ltd. Tel: +356 21 44 7184

GALVUS and EUCREAS
COMPREHENSIVE POWER TO ADVANCE TYPE 2 DIABETES TREATMENT

GALVUS is a DPP-4 inhibitor that improves glycemic control through powerful islet enhancement[1]

EUCREAS is the combination of a DPP-4 inhibitor, GALVUS, and metformin[2]

Galvus®
PRESENTATION: Each tablet contains 50 mg of Vildagliptin. **INDICATIONS:** For the treatment of type 2 diabetes mellitus in adults. As monotherapy in patients inadequately controlled by diet and exercise alone and for whom metformin is inappropriate due to contraindications or intolerance. As dual oral therapy in combination with metformin in patients with insufficient glycaemic control despite maximal tolerated dose of monotherapy with metformin; a sulphonylurea in patients with insufficient glycaemic control despite maximal tolerated dose of a sulphonylurea and for whom metformin is inappropriate due to contraindications or intolerance; a thiazolidinedione in patients with insufficient glycaemic control and for whom the use of a thiazolidinedione is appropriate. As triple oral therapy in combination with a sulphonylurea and metformin when diet and exercise plus dual therapy with these medicinal products do not provide adequate glycaemic control. Vildagliptin is also indicated for use in combination with insulin (with or without metformin) when diet and exercise plus a stable dose of insulin do not provide adequate glycaemic control. **DOSAGE:** When used as monotherapy or combination with thiazolidinedione, in combination with metformin and a sulphonylurea or in combination with insulin (with or without metformin): the recommended daily dose of Vildagliptin is 100mg, administered as one dose of 50 mg in the morning and one dose of 50 mg in the evening. When used in combination with a sulphonylurea, a lower dose of the sulphonylurea may be considered to reduce the risk of hypoglycaemia. Galvus can be administered with or without a meal. Doses greater than 100 mg are not recommended. Galvus is not recommended for use in children and adolescents (< 18 years). The safety and efficacy of Galvus in children and adolescents (< 18 years) have not been established. No data are available. The recommended dose for patients with moderate/severe renal impairment is 50mg once daily. For dose of Galvus in elderly patients (≥ 65 years). The safety and efficacy of Vildagliptin as triple oral therapy in combination with metformin and a thiazolidinedione have not been established. **CONTRAINDICATIONS:** Hypersensitivity to the active substance or to any of the excipients mentioned. **PRECAUTIONS:** Galvus should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis. There is limited experience in patients with NYHA functional class III cardiac disease. Therefore Galvus should be used with caution in these patients. Galvus is not recommended in patients with hepatic impairment, including patients with pre-treatment ALT or AST >3x the ULN. Liver function tests should be performed prior to treatment initiation, at three month intervals during the first year and periodically thereafter. Should an increase in AST or ALT of 3xULN or greater persist, withdrawal of Galvus therapy is recommended. Patients who develop jaundice or other signs suggestive of liver dysfunction should discontinue Galvus. Clinical experience in patients with NYHA functional class III treated with Vildagliptin is still limited and results are monitored. Routine monitoring of diabetic patients for skin disorders such as blistering or ulceration is recommended. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine. Galvus should not be administered during pregnancy or breast-feeding since no studies on the effect on human fertility have been conducted for Galvus. Should be used with caution in patients with renal impairment. Sulphonylureas are known to cause hypoglycaemia. Patients receiving Vildagliptin in combination with a sulphonylurea may be at risk for hypoglycaemia. Therefore, a lower dose of sulphonylurea may be considered to reduce the risk of hypoglycaemia. Use of Vildagliptin has been associated with a risk of developing acute pancreatitis. If pancreatitis is suspected, Vildagliptin should be discontinued. If acute pancreatitis is confirmed, Vildagliptin should not be restarted. Caution should be exercised in patients with a history of acute pancreatitis. **INTERACTIONS:** Vildagliptin has a low potential for drug interactions. No clinically relevant interactions with other antidiabetics (glibenclide, pioglitazone, metformin, amlodipine, digoxin, ramipril, simvastatin, valsartan or warfarin) were observed after co-administration with Vildagliptin. As with other oral antidiabetic medicines, the hypoglycaemic effect of Vildagliptin may be reduced by certain active substances including thiazides, corticosteroids, thyroid products and sympathomimetics. **ADVERSE REACTIONS:** Rare cases (>1/10,000 to <1/1,000) angioedema, abnormal liver function tests, hepatic dysfunction (including hepatitis). Mixed therapy: Common (>1/100 to <1/10): dizziness, Uncommon (>1/1,000 to <1/100): headache, constipation, arthralgia, hypoglycaemia, oedema peripheral. Very rare (<1/10,000): URTI, nasopharyngitis. Combination with metformin: Common: tremor, headache, dizziness, nausea, hypoglycaemia, hyperhidrosis, asthenia. Uncommon: fatigue. Combination with sulphonylurea: Common: tremor, headache, dizziness, asthenia, hypoglycaemia. Uncommon: constipation. Very rare: nasopharyngitis. Combination with Thiazolidinediones: Common: weight increase, oedema peripheral. Uncommon: headache, asthenia, hypoglycaemia. Combination with Insulin: Common: decreased blood glucose, headache, vertigo, nausea, gastro-oesophageal reflux disease. Uncommon: Diarrhoea, flatulence. Frequency and kinetics: amylase, pancreatitis, hepatitis and abnormal liver function tests. Immediate upon discontinuation of the medicinal products: bullous or exfoliative skin lesions. Combination with metformin and a sulphonylurea: Common: hypoglycaemia, dizziness, tremor, hyperhidrosis, asthenia. **LEGAL CATEGORY:** POM **PACK SIZES:** 7, 28 tablets **MARKETING AUTHORISATION HOLDER:** Novartis Europharm Limited, Primary Business Park Castleisland Co.Kerry Ireland. **MARKETING AUTHORISATION NUMBERS:** EU/1/07/414/001-002
Please refer to Summary of Product Characteristics (SmPC) before prescribing. Full prescribing information is available on request from Novartis Pharma Services Inc, Representative Office Malta, P.O. Box 4, Marsa, MRS 1000, Malta. Tel +356 21222872. 2015-MT-GAL-19-JUN-2015

Eucreas®
PRESENTATION: Each 50 mg/850 mg film-coated tablet contains 50 mg of vildagliptin and 850 mg metformin hydrochloride. Each 50 mg/1000 mg film-coated tablet contains 50 mg of vildagliptin and 1000 mg metformin hydrochloride. **INDICATIONS:** Eucreas is indicated in the treatment of type 2 diabetes mellitus patients who are unable to achieve sufficient glycaemic control at their maximally tolerated dose of oral metformin alone or who are already treated with the combination of vildagliptin and metformin as separate tablets. Eucreas is indicated in combination with a sulphonylurea (i.e. triple combination therapy) as an adjunct to diet and exercise in adult patients inadequately controlled with metformin and a sulphonylurea. Eucreas is indicated in triple combination therapy with insulin as an adjunct to diet and exercise to improve glycaemic control in adult patients when insulin at a stable dose and metformin alone do not provide adequate glycaemic control. **DOSAGE:** The dose of antihyperglycaemic therapy with Eucreas should be tailored based on the basis of the patient's current regimen, effectiveness and tolerability while not exceeding the maximum recommended daily dose of 100 mg vildagliptin. Eucreas may be initiated at either the 50 mg/850 mg or 50 mg/1000 mg dose strength twice daily, one tablet in the morning and the other in the evening. For patients inadequately controlled at their maximal tolerated dose of metformin monotherapy: The starting dose of Eucreas should provide vildagliptin at 50 mg twice daily (100 mg total daily dose) plus the dose of metformin already being taken. For patients switching from co-administration of vildagliptin and metformin as separate tablets: Eucreas should be initiated at the dose of vildagliptin and metformin already being taken. For patients inadequately controlled on dual combination therapy with metformin and a sulphonylurea: The dose of Eucreas should provide vildagliptin at 50 mg twice daily (100 mg total daily dose) and a dose of metformin similar to the dose already being taken. When Eucreas is used in combination with a sulphonylurea, a lower dose of the sulphonylurea may be considered to reduce the risk of hypoglycaemia. For patients inadequately controlled on dual combination therapy with insulin and the maximal tolerated dose of metformin: The dose of Eucreas should provide vildagliptin at 50 mg twice daily (100 mg total daily dose) and a dose of metformin similar to the dose already being taken. Eucreas should be taken with or just after food to reduce gastrointestinal symptoms associated with metformin. Patients 65 taking Eucreas should have their renal function monitored regularly. Eucreas is not recommended for use in patients less than 18 years old. For use in renal or hepatic impairment, see contraindications and precautions below or refer to the SmPC for triple combination. The safety and efficacy of vildagliptin and metformin as triple oral therapy in combination with a thiazolidinedione have not been established. **CONTRAINDICATIONS:** Hypersensitivity to vildagliptin or metformin hydrochloride or to any of the excipients. Diabetic ketoacidosis or diabetic pre-coma. Renal failure or renal dysfunction defined as creatinine clearance < 60 ml/min. Acute conditions with the potential to alter renal function e.g. dehydration, severe infection, shock or intravascular administration of iodinated contrast agents. Acute or chronic disease which may cause tissue hypoxia e.g. cardiac or respiratory failure, recent myocardial infarction, shock. Hepatic impairment, acute alcohol intoxication, alcoholism. Lactation. **WARNINGS / PRECAUTIONS:** Eucreas is not a substitute for insulin in insulin-requiring patients and should not be used in patients with type 1 diabetes. Due to the risk of lactic acidosis, renal function must be monitored at least annually in patients with normal renal function and at least two to four times/year in patients with serum creatinine at the upper limit of normal and in elderly patients. Eucreas is not recommended in patients with hepatic impairment, including patients with pre-treatment ALT or AST >3x the ULN. If a stable but chronic elevation of liver transaminases is found, dose reduction or withdrawal of Eucreas should be considered. Eucreas should be withheld for at least 48 hours before elective surgery with general anaesthesia and not usually resumed earlier than 48 hours afterwards. The co-administration of iodinated contrast agents can lead to renal failure. Therefore due to metformin active ingredient, Eucreas should be discontinued prior to or at the time of the test and not reinstituted until 48 hours afterwards and only after renal function has been re-evaluated and found to be normal. Eucreas should not be administered during pregnancy or lactation. Sulphonylureas are known to cause hypoglycaemia. Patients receiving vildagliptin in combination with a sulphonylurea may be at risk for hypoglycaemia. Therefore, a lower dose of sulphonylurea may be considered to reduce the risk of hypoglycaemia. The use of vildagliptin has been associated with a risk of developing acute pancreatitis. If pancreatitis is suspected, vildagliptin should be discontinued. If acute pancreatitis is confirmed vildagliptin should not be restarted. Caution should be exercised in patients with a history of acute pancreatitis. **INTERACTIONS:** Vildagliptin has a low potential for drug interactions. No clinically relevant interactions with other antidiabetics (glibenclide, pioglitazone, metformin, amlodipine, digoxin, ramipril, simvastatin, valsartan or warfarin) were observed after co-administration with vildagliptin. As with other oral antidiabetic medicines, the hypoglycaemic effect of vildagliptin may be reduced by certain active substances including thiazides, corticosteroids, thyroid products and sympathomimetics. Alcohol: caution active substances (e.g. cimetidine) and intravascular administration of iodinated contrast media. Combinations requiring caution include metformin hydrochloride with medicines forming to produce hyperglycaemia (e.g. thiazides and other diuretics, corticosteroids, beta agonists and diuretics). The dose of antihyperglycaemic medicinal products may need to be adjusted in combination with ACE inhibitors. **ADVERSE REACTIONS:** Rare cases (>1/10,000 to <1/1,000): angioedema, hepatic dysfunction (including hepatitis) have been reported with vildagliptin. Vildagliptin Monotherapy: Common (>1/100 to <1/10): dizziness, Uncommon (>1/1,000 to <1/100): headache, constipation, arthralgia, hypoglycaemia, oedema peripheral. Very rare (<1/10,000): URTI, nasopharyngitis. Metformin monotherapy: Very common (>1/10): nausea, vomiting, diarrhoea, abdominal pain and loss of appetite. Common: metallic taste. Combination vildagliptin with metformin: Common: tremor, headache, dizziness, nausea. Hypoglycaemia, hyperhidrosis, asthenia with metformin and sulphonylurea: Common: hypoglycaemia. Dizziness, tremor, hyperhidrosis, asthenia, decreased blood glucose, headache, data. Combination with insulin: Decreased blood glucose, hypoglycaemia, vertigo, nausea, gastro-oesophageal reflux disease, diarrhoea, flatulence. For a full list of Eucreas reactions, please refer to the SmPC. **LEGAL CATEGORY:** POM **PACK SIZES:** 30, 60 film-coated tablets. **MARKETING AUTHORISATION HOLDER:** Novartis Europharm Limited, Frimley Business Park, Camberley GU16 7SR, United Kingdom. **MARKETING AUTHORISATION NUMBER:** EU/1/07/402/003-006, EU/1/07/402/009-012
Please refer to Summary of Product Characteristics (SmPC) before prescribing. Full prescribing information is available upon request from Novartis Pharma Services Inc, Representative Office Malta, P.O. Box 4, Marsa, MRS 1000, Malta. Tel +356 21222872. 2015-MT-GAL-19-JUN-2015

GAL Ad1 11/15 MT

Galvus vildagliptin

Eucreas vildagliptin/metformin

NOVARTIS PHARMACEUTICALS

1. Novartis Europharm Ltd. Galvus® Summary of Product Characteristics
2. Novartis Europharm Ltd. Eucreas® Summary of Product Characteristics

SONIA VANCELL &
FRANCO VASSALLO

NEGLIGENCE AND CIVIL LIABILITY IN THE MEDICAL PROFESSION - PART I

Liability in the medical profession arises when the patient is not treated according to acceptable standard of care. It is a well-known fact that the medical professional is not duty bound to give specific results. The medical professional is however obliged to carry out the treatment to the best of his capabilities. The principal aim of this article is to analyse what constitutes negligence and when liability arises. Besides considering the defences that can be raised in a law suit for medical malpractice, this article will also make reference to the opinions and decisions of Maltese courts.

A. DUTY OF CARE AND CONTRACTUAL DUTIES IN THE FIELD OF MEDICAL LAW

The nature of the relationship between doctors and patients is determined largely by practice of the profession and is shaped by a strong commitment towards long-standing principles of medical ethics. The law plays a significant role in providing a structure within which the doctor-patient relationship is conducted. Legal rules set out a minimum standard of professional behaviour. Ideal standards of practice are left to the profession itself to define. The law only comes into play in case of dispute where, the patient or his successors claim that such minimum standards have not been attained.

B. CONTRACTUAL AND TORTIOUS RESPONSIBILITY UNDER MALTESE LAW

B.I. CONTRACT OR TORT?

The doctor-patient relationship may be based either upon a contract between the parties, upon an undertaking to perform or on both. Given this dual source of doctor-patient relationship, a question arises, that is whether tort or contract law governs the rights and liabilities of the parties.

In the Maltese legal scenario, for a person to incur responsibility, there must have been a breach of a contractual obligation which can be raised tacitly or implicitly, or else a breach of an obligation imposed by law.

The doctor is required to follow the applicable standard of care not only when he impliedly agrees to do so, but also in view of the fact that the medical professional is obliged to do so by law. Even though an aggrieved party can choose whether to sue the alleged offendor on the basis of a breach of contract or on the basis of a breach of a duty imposed upon him by law, there has been a general trend that whenever there is an allegation that a medical professional has failed to exercise the mandatory degree of care, tort law rather than contract law provides the basis for the claim. This notwithstanding, regardless of whether the physician-patient relationship is based on a contract or not, the duty of care is the same.

[WHEN JUDGING ON NEGLIGENCE AND CIVIL LIABILITY] THE COURT MUST RELY ON OTHER MEMBERS OF THE [MEDICAL] PROFESSION...

B.II. MAIN DIFFERENCES BETWEEN CONTRACTUAL AND TORTIOUS RESPONSIBILITY

Primarily, whereas the person breaching a contractual obligation specifically provided for in a contract binding the parties would incur contractual responsibility, any person violating an obligation imposed by the law would incur tortious responsibility. This notwithstanding, the result remains the same, namely that of being held responsible for the violation of a contractual or a legal obligation.

Another important distinction between contractual and tortious responsibility lies in the effects such breach has on the person found responsible. In contractual responsibility the person whose rights have been breached may invoke the primary effect of the obligation, in other words compel the other party to perform the obligation that he had undertaken. The aggrieved party may on the other hand sue the defaulting party for damages arising out of breach of contract. In tortious responsibility the only remedy available to the injured party is suing the offender for the recovery of damages caused by the tortious act.

In furtherance, the Civil Code (Chapter 16 of the Laws of Malta) provides that an action for damages arising out of non-performance of a contractual obligation is time-barred by the lapse of 5 years. An action for damages arising out of tort is time-barred by a lapse of 2 years.

C. ELEMENTS OF NEGLIGENCE

A claim of breach of contract or of a breach of a duty imposed by law based on negligence can be successful, if the patient proves to the satisfaction of the court the three main elements of negligence, that is that:

i. the physician had a duty of care in that particular situation
ii. the physician failed to discharge the standard of care required by that duty and
iii. he has suffered damages in consequence of a breach of that duty.

...DAMAGES ARISING OUT OF NON-PERFORMANCE OF A CONTRACTUAL OBLIGATION IS TIME-BARRED BY THE LAPSE OF 5 YEARS. AN ACTION FOR DAMAGES ARISING OUT OF TORT IS TIME-BARRED BY A LAPSE OF 2 YEARS

C.I DUTY OF CARE

This refers to the fact that the doctor has a duty to provide the patient with care in accordance with an accepted standard.

C.II BREACH OF DUTY

C.ii.a Standard of Care

Article 1132(1) of the Civil Code (Chapter 16 of the Laws of Malta) provides that:

*"... the degree of diligence to be exercised in the performance of any obligation, whether the object thereof is the benefit of only one of the parties, or of both, is, in all cases, that of a **bonus paterfamilias** as provided in section 1032." emphasis added*

Article 1032, establishes that:

*"A person shall be deemed to be in fault if, in his own acts, he does not use the prudence, diligence, and attention of a **bonus paterfamilias**." emphasis added*

These provisions establish that the standard of care required in contract and tort law is that of the diligence of a bonus paterfamilias. In the medical profession this has been tied to the responsibility of a reasonable man exercising and professing to have that special skill.

This doctrine has been taken a step forward to include the notion of accepted practice in the medical profession as one which is highly specialised and therefore the court must rely on other members of the profession and their behaviour in given circumstances to be able to compare and judge the treatment given. As will be described in further detail in the next article, the notion of accepted practice is fundamental as the courts must endeavour to avoid curtailing the development of medical science and in fact one can observe an effort to strike a balance between the progress of medical science and the protection of patients.

(to be continued ...)

The Powerful Amoxicillin + Clavulanic Acid Combination

Forcid Solutab®:

- Contains amoxicillin and clavulanic acid in the ratio 7:1, the powerful combination to fight infections in unique Solutab® formulation

Forcid Solutab® indications:

- Acute bacterial sinusitis, acute otitis media, acute exacerbations of chronic bronchitis, community acquired pneumonia.
- Cystitis, pyelonephritis.
- Skin and soft tissue infections in particular cellulitis, animal bites.
- Severe dental abscess with spreading cellulitis.
- Bone and joint infections, in particular osteomyelitis.

Forcid Solutab® offers a convenient antibiotic therapy for adults and children:

- Easy and flexible administration, the unique versatile formulation can be swallowed intact or dissolved in water.
- Equally effective whether dissolved in water or taken as a tablet and rapidly absorbed.[1]
- Suitable for a wide range of patients: no sugar, no gluten, no sodium, no lactose.

Forcid Solutab® dosing in adults and children ≥ 40 kg:

- Standard dose of Forcid Solutab 1000 is 2 times a day.
- For infections such as otitis media, sinusitis, lower respiratory tract infections and urinary tract infections, Forcid Solutab1000 is recommended to be given 3 times per day.

Forcid® 1000 Abbreviated Prescribing Information. Presentation: Forcid® 1000, containing as active substances amoxicillin and clavulanic acid. Each tablet/dispersible tablet contains 875 mg amoxicillin as amoxicillin trihydrate and 125 mg clavulanic acid as potassium clavulanate. **Indications:** Amoxicillin/clavulanic acid tablets are indicated for the treatment of the following infections in adults and children: acute bacterial sinusitis (adequately diagnosed), acute otitis media, acute exacerbations of chronic bronchitis (adequately diagnosed), community acquired pneumonia, cystitis, pyelonephritis, skin and soft tissue infections in particular cellulitis, animal bites, severe dental abscess with spreading cellulitis, bone and joint infections, in particular osteomyelitis. Consideration should be given to official guidance on the appropriate use of antibacterial agents. **Duration of therapy:** The duration of therapy should be determined by the response of the patient. Some infections (e.g. osteomyelitis) require longer periods of treatment. Treatment should not be extended beyond 14 days without review. **Posology:** The dose of amoxicillin/clavulanic acid that is selected to treat an individual infection should take into account the expected pathogens and their likely susceptibility to antibacterial agents, the severity and site of infection, the age, weight and renal function of the patient. **Adults and children over 40 kg:** The standard dose of Forcid 1000 is 2 times a day. For infections such as otitis media, sinusitis, lower respiratory infections and urinary tract infections, Forcid 1000 is recommended to be given 3 times per day. **Children under 40 kg:** 25mg/3.6mg/kg/day to 45mg/6.4mg/kg/day given as 2 divided doses. No clinical data are available for amoxicillin/clavulanic acid 7:1 formulations higher than 45mg/6.4mg/kg per day in children under 2 years. There are no clinical data for amoxicillin/clavulanic acid 7:1 formulations for patients under 2 months of age. Dosing recommendations in this population cannot be made. **Elderly patients:** No dose adjustment is necessary. **Patients with impaired renal function:** No dose adjustment in dose required in patients with creatinine clearance (CrCl) greater than 30ml/min. In patients with CrCl less than 30ml/min, use of Forcid 1000 is not recommended as no recommendations for dose adjustments are available. **Patients with impaired liver function:** Dose with caution and monitor hepatic function at regular intervals. **Method of administration:** Amoxicillin/clavulanic acid tablets are for oral use. Administer at the start of a meal to minimise potential gastrointestinal intolerance and optimise absorption. Forcid tablets can be swallowed whole with a glass of water, or first dissolved in a ½ cup of water (at least 30ml) and stirred thoroughly before swallowing. **Contraindications:** Hypersensitivity to the active substances, to any penicillins or to any of the excipients. History of severe immediate hypersensitivity reaction (e.g. anaphylaxis) to another beta-lactam agent (e.g. a cephalosporin, carbapenem or monobactam). History of jaundice/hepatic impairment due to amoxicillin/clavulanic acid. **Special warnings and precautions for use:** Before initiating therapy, careful enquiry should be made of previous hypersensitivity reactions to penicillins, cephalosporins or other beta-lactam agents. Serious and occasionally fatal hypersensitivity (anaphylactoid) reactions have been reported in patients on penicillin therapy. These reactions are more likely to occur in patients with a history of penicillin hypersensitivity and in atopic individuals. If an allergic reaction occurs, amoxicillin/clavulanic acid must be discontinued and appropriate alternative therapy instituted. If an infection is proven to be due to amoxicillin-susceptible organism(s), consideration should be given to switching from amoxicillin/clavulanic acid to amoxicillin in accordance with official guidance. This presentation of amoxicillin/clavulanic acid is not suitable for use when there is high risk that presumptive pathogens have resistance to beta-lactam agents that is not mediated by beta-lactamases susceptible to inhibition by clavulanic acid. This presentation should also not be used to treat penicillin-resistant *S. pneumonia*. Convulsions may occur in patients with impaired renal function or in those receiving high doses. Avoid if infectious mononucleosis is suspected. Concomitant use of allopurinol during treatment with amoxicillin can increase the likelihood of allergic skin reactions. Prolonged use may result in overgrowth of non-susceptible organisms. Occurrence of feverish generalised erythema associated with pustula at treatment initiation may be a symptom of acute generalised exanthemous pustulosis (AGEP) and requires treatment discontinuation and contra-indicates any subsequent administration of amoxicillin. Use with caution in patients with evidence of hepatic impairment. Hepatic events have been reported predominantly in males and elderly patients and may be associated with prolonged treatment. These events have been very rarely reported in children. In all populations, signs and symptoms usually occur during or shortly after treatment but in some cases may not become apparent until several weeks after treatment has ceased. These are usually reversible. Hepatic events may be severe and in extremely rare circumstances, deaths have been reported. These have almost always occurred in patients with serious underlying disease or taking concomitant medications known to have the potential for hepatic effects. Antibiotic-associated colitis has been reported, consider in patients who present with diarrhoea. Should antibiotic-associated colitis occur, amoxicillin/clavulanic acid should immediately be discontinued, a physician be consulted and an appropriate therapy initiated. Anti-peristaltic medicinal products are contra-indicated in this situation. Periodic assessment of organ system functions is advisable during prolonged therapy. Prolongation of prothrombin time was reported rarely in patients receiving amoxicillin/clavulanic acid. Appropriate monitoring should be undertaken when anticoagulants are prescribed concomitantly. Adjustments in the dose of oral anticoagulants may be necessary to maintain the desired level of anticoagulation. In patients with renal impairment, dose should be adjusted according to degree of impairment. In patients with reduced urine output, crystalluria has been observed very rarely, mainly with parenteral therapy. Maintain adequate fluid intake and urinary output during administration of high doses of amoxicillin to reduce possibility of amoxicillin crystalluria. If bladder catheter is in-situ, check patency. False positive results may occur when testing presence of glucose in urine with non-enzymatic methods during treatment of amoxicillin; use enzymatic glucose oxidase methods. Clavulanic acid in Forcid may cause non-specific binding of IgG and albumin by red cell membranes leading to false positive Coombs test. Reports of positive test results using Bio-Rad Laboratories Platelia *Aspergillus* EIA test; cross-reactions with non-*Aspergillus* polysaccharides and polyfuranoses with Bio-Rad Laboratories Platelia *Aspergillus* EIA test have been reported; positive results should be interpreted cautiously and confirmed by other diagnostic methods. Forcid 1000 contains 0.64 mmol potassium per tablet (25 mg). **Pregnancy and lactation:** Use in pregnancy should be avoided unless considered essential by physician. Both amoxicillin and clavulanic acid are excreted in breast milk; consequently diarrhoea and fungus infection of mucous membranes is possible in breast-fed infants. Amoxicillin/clavulanic acid should only be used during breast-feeding after benefit/risk assessment by physician in charge. **Undesirable effects:** The most commonly reported adverse reactions (ADRs) are diarrhoea, nausea and vomiting. For a full listing of undesirable effects, refer to the complete Summary of Product Characteristics for Forcid 1000. Marketing authorization holder: Astellas Pharma Europe BV., Sylviusweg 62, 2333 BE Leiden. The Netherlands. 13-FOR-003 Adverse events should be reported to the local regulatory authority and Astellas Pharma Europe BV., Sylviusweg 62, 2333 BE Leiden. The Netherlands. Please read carefully the instructions on the package leaflet. 13-FOR-004 102013

Reference: 1. H. Sourgens et al. International Journalof Clinical Pharmacology and Therapeutics. 2004; 42: 165-173.

astellas
Leading Light for Life

Amoxicillin clavulanic acid
FORCID Solutab®

Relvar Ellipta is for patients (≥12 years) in need of asthma maintenance therapy[1]

Asthma

Because I simply don't have space for asthma

For patients like Maria, every day is full on, so even small reminders of asthma can have an impact. So, when they're uncontrolled on ICS alone, choose new Relvar Ellipta:

- The first ICS/LABA combination to deliver continuous 24-hour efficacy[2]
- In a practical, once-daily dose[1]
- Delivered in an easy to use device that patients prefer to their current inhaler[3,4*]

RELVAR® ELLIPTA®

(fluticasone furoate and vilanterol inhalation powder)

Practical efficacy

Relvar Ellipta (fluticasone furoate/vilanterol) Abridged Prescribing Information

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 on SPC how to report adverse reactions.

Please refer to the full Summary of Product Characteristics before prescribing

Trade Name: RELVAR ELLIPTA. **Active Ingredients:** 92 micrograms or 184 micrograms of fluticasone furoate and 22 micrograms of vilanterol (as trifenatate). **Pharmaceutical Form:** 92 micrograms/22 micrograms or 184 micrograms/22 micrograms inhalation powder, pre-dispensed. **Indications:** *The 92 micrograms/22 micrograms dose:* for the regular treatment of asthma in adults and adolescents aged 12 years and older where use of a combination medicinal product (long-acting $beta_2$-agonist and inhaled corticosteroid) is appropriate; and for the symptomatic treatment of adults with COPD with a FEV_1<70% predicted normal (post-bronchodilator) with an exacerbation history despite regular bronchodilator therapy. *The 184 micrograms/22 micrograms dose:* for the regular treatment of asthma in adults and adolescents aged 12 years and older where use of a combination medicinal product (long-acting $beta_2$-agonist and inhaled corticosteroid) is appropriate. **Dosage and Method of Administration:** *For Athsma:* One inhalation of Relvar Ellipta 92/22 micrograms or 184/22 micrograms once daily. Patients usually experience an improvement in lung function within 15 minutes of inhaling Relvar Ellipta. However, the patient should be informed that regular daily usage is necessary to maintain control of asthma symptoms and that use should be continued even when asymptomatic. If symptoms arise in the period between doses, an inhaled, short-acting $beta_2$-agonist should be taken for immediate relief. A starting dose of Relvar Ellipta 92/22 micrograms should be considered for adults and adolescents 12 years and over who require a low to mid dose of inhaled corticosteroid in combination with a long-acting $beta_2$-agonist. If patients are inadequately controlled on Relvar Ellipta 92/22 micrograms, the dose can be increased to 184/22 micrograms, which may provide additional improvement in asthma control. *For COPD:* One inhalation of Relvar Ellipta 92/22 micrograms once daily. Relvar Ellipta 184/22 micrograms is not indicated for patients with COPD. Relvar Ellipta is for inhalation use only. It should be administered at the same time of the day, each day. **Contraindications:** *Hypersensitivity* to the active ingredient or excipients. **Precautions for Use:** Fluticasone furoate/vilanterol should not be used to treat acute asthma symptoms, for which a short-acting bronchodilator is required. Caution in severe cardiovascular disease, moderate-to-severe hepatic impairment, pulmonary tuberculosis or in patients with chronic or untreated infections, history of diabetes mellitus and for paradoxical bronchospasm and pneumonia in patients with COPD. **Drug Interactions:** Beta-blockers, CYP3A4 inhibitors, P-glycoprotein inhibitors and sympathomimetic medicinal products (refer to the full Summary of Product Characteristics for list of drugs). **Fertility, Pregnancy and Lactation:** ***Pregnancy:*** No adequate data available. ***Lactation:*** insufficient information available. ***Fertility:*** There is no data in humans. Animal studies indicate no effect on fertility. **Effect on Ability to Drive or Use Machines:** No or negligible influence. **Undesirable Effects:** Very common side effects include headache and nasopharyngitis (refer to the full Summary of Product Characteristics for complete list of undesirable effects). **Overdose:** There is no specific antidote. Treatment of overdose should consist of general supportive measures. **Local Presentations:** Relvar Ellipta 92 micrograms/22 micrograms inhalation powder, pre-dispensed and Relvar Ellipta 184 *micrograms/ 22 micrograms inhalation powder, pre-dispensed*. **Legal Category:** POM. **Marketing Authorisation Holder:** Glaxo Group Limited, 980 Great West Road, Brentford, Middlesex TW8 9GS, United Kingdom **Marketing Authorisation Numbers:** EU/1/13/886/001-6 **DATE OF PREPARATION:** December 2013

In order to ensure that this product information reflects the mos up-to-date clinical and post-marketing surveillance data, please always refer to the latest Summary of Product Characteristics (SPC) which is available from GlaxoSmithKline (Malta) Ltd (Tel: +356 21238131)

REPORTING ADVERSE EVENTS (AEs):

Malta & Gibraltar: **If you become aware of any AEs, medication errors and/or use during pregnancy in association with GSK products, please report the event promptly to:** GSK (Malta) Limited, 1, De la Cruz Avenue, Qormi QRM 2458, Malta (Tel: +356 21238131)

Malta: **alternatively, any suspected AEs and medication errors can also be reported via the national Adverse Drug Reactions (ADRs) reporting system**

Report forms can be downloaded from www.medicinesauthority.gov.mt/adrportal and posted to the Malta Medicines Authority, Post-licensing Directorate, 203, Level 3, Rue D'Argens, Gżira GŻR 1368, MALTA, or sent by email to postlicensing.medicinesauthority@gov.mt

Gibraltar: **alternatively, any suspected AEs and medication errors can also be reported via the UK regulatory authority (MHRA):** https://yellowcard.mhra.gov.uk/

*Patients' current or previous maintenance inhalers: HandiHaler/ DISKUS/ MDI/ HFA (COPD); DISKUS/ MDI/ HFA (asthma).[4]

References: 1. Relvar Ellipta Summary of Product Characteristics. GlaxoSmithKline; 2013. **2.** Bleecker ER *et al.* Fluticasone furoate/vilanterol 100/25 mcg compared with fluticasone furoate 100 mcg in asthma: a randomized trial. *JACI In Practice* 2013 (in press). **3.** Svedstater H *et al.* Ease of use of a two-strip dry powder inhaler (DPI) to deliver fluticasone furoate/ vilanterol (FF/VI) and FF alone in asthma. ERS. 2013. **4.** Woepse M *et al.* Qualitative assessment of a two-strip dry powder inhaler (ELLIPTA™) for COPD and asthma. EAACI. 2013.

MLT_GIB/RESP/0006/14 Date of preparation: January 2014

gsk

Theravance

PITFALLS IN DEATH CERTIFICATION

KATHLEEN ENGLAND

ABSTRACT

Apart from their administrative purpose, death certificate data are a major means of identifying public health problems and evaluating the effectiveness of programs developed to deal with these public health problems. The inaccuracies in death certification are well documented in the international literature. This study aimed to estimate the accuracy in cancer death certification locally, as well as present common types of errors in order to create educational awareness.

INTRODUCTION

Without health data, governments and other organisations cannot accurately target resources to prevent deaths and diseases, and have no way to measure whether their efforts are working.[1] Mortality data obtained from information recorded on the death certificate is one of the oldest sources of health data. Published mortality data for Malta, by cause of death are available since 1872. These were produced in the form of a fortnightly report published by the Chief Police Physician. Annual reports after 1896 were published by the Chief Government Medical Officer.

Mortality data is a source of information used:

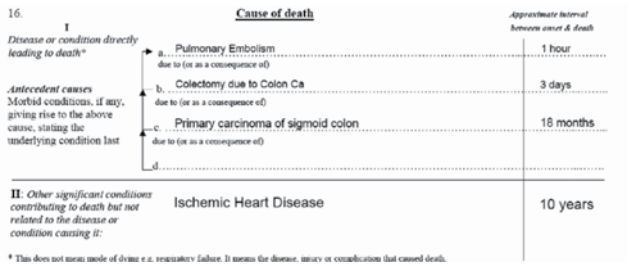
1. To monitor trends and patterns in disease;
2. To guide health promotion, resource allocation, service planning and priority determination;
3. For research and epidemiology; and
4. For administrative purposes including settlement of estates, welfare and pension entitlements and insurance payment.[2]

Mortality statistics are mainly based on the ***'underlying cause of death'*** which is defined as "(a) the disease or injury which initiated the train of morbid events leading directly to death, or (b) the circumstances of the accident or violence which produced the fatal injury".[3] This is because from the standpoint of prevention of death, it is necessary to break the chain of events or to effect a cure at some point. The most effective public health objective is to prevent the precipitating cause from operating.

For this reason, section 16 of the Medical Death Certificate is divided into two parts with **part I** relating to the train of events leading directly to death, and **part II** concerns unrelated but contributory conditions. The condition recorded on the **lowest used line of part I** of the certificate is usually the underlying cause of death used for tabulation, if the death certificate is completed accurately.

Despite the importance of accurate death certification, errors are common. International studies report inaccuracies in death certificates to be 20-65%.[4,5] In a previous local study (by the author, unpublished), it was found that 37% of death certificates reviewed were found to have a major error which means that coders had difficulty in choosing the correct underlying cause of death. The variable which was most significantly associated with a major error rate was age of the deceased.

Figure 1: Example of a completed medical section of the death certificate



AIM

The aim of the study was to review all death certificates in 2013 and estimate the accuracy in cancer death certification. The common types of errors are presented in order to create educational awareness.

METHODOLOGY

All death certificates of deaths registered during 2013 were reviewed and the main cause of death according to the certifier was extracted. Where the main cause of death was certified to be cancer, the death certificate was reviewed and additional information obtained by linking with the National Cancer Registry, seeking histology and radiological information from ISOFT and accessing the electronic case summary of the patient to confirm or otherwise the cancer and the underlying cause of death.

RESULTS

In all there were 888 death certificates which were classified as a cancer death i.e. a particular cancer was recorded by the certifier as the main or underlying cause of death. Of these, 796 certificates or 89.6% were confirmed to be correct. As seen in table 1 below, the error rate increased with age of the deceased. This is attributed to the fact that often in the elderly, competing causes may exist and the certifier may be unsure what was the main or underlying cause of death.

Table 1: Number and % of major errors in cancer death certification

Age Group	number of major errors	correct	Total death certificates	% error
<65	14	207	221	6.3
65-74	13	232	245	5.3
75-84	23	161	184	12.5
>85	42	196	238	17.6
Total	**92**	**796**	**888**	**10.4**

The percentage of incorrectly completed death certificates involving a cancer as a main cause was higher in death certificates certified by general practitioners compared to those certified by hospital doctors (14% versus 10%). This can be generally attributed to less accurate information being available to the general practitioner versus the hospital doctor. Furthermore, the proportion of death certificates certified by general practitioner increases in the elderly and decreases for hospital doctors.

The main errors identified were:

1. Conflicting causes of death written in part I of section 16

e.g. Metastasis
Ca Bladder and Ca Colon } Which cancer is responsible for the metastasis?

2. Conflicting causes of death and wrong sequence of events listed in part I of section 16

e.g. Chest Infection
Dementia
Breast Cancer
Diabetes mellitus } Which direct sequence of events lead to the death of the patient? All other conditions should be put in part II

3. Wrong cancer written down on the death certificate

- "Metastasis" without identification of primary site should only be written when there is no known primary site and this should be stated.
- When there is metastasis to the lung, the certifier should write "Metastasis to the lung with unknown primary". In this case, reporting "Carcinoma Lung" is incorrect as the coder would not know if it is a primary or due to metastasis.
- "Carcinoma oesophagus" should not be written when the primary site of the carcinoma is the stomach.
- When writing "liver cancer" one should always specify whether it is primary or secondary.

4. No evidence of cancer

In a few of the certificates reviewed, especially in elderly persons, there was mention of a cancer with no evidence found by the coder.

A number of other minor errors have also been identified which include absence of time intervals between onset and death and lack of specificity about the tumour. E.g. "Adeno-carcinoma of the sigmoid colon" should be written rather than "cancer of the colon"; "Left frontal lobe primary malignant tumour of brain consistent with astrocytoma" should be written instead of "brain tumour".

DISCUSSION AND CONCLUSIONS

In a previous local study (by the author, unpublished), high levels of agreement between the certifier and the medical notes were found for neoplasms (92%), cerebrovascular disease (92%) and chronic lower respiratory diseases (86%). Lower levels of agreement were found for Ischaemic heart disease (78%), pneumonia (58%) and diabetes mellitus (31%).

The reported rate for neoplasms (92%) is similar to that found in this study (89.6%) and highlights the fact that deaths from neoplasms tend to be more straightforward than other conditions which involve multiple co-morbidity.

Often physicians enter correct diagnoses on the death certificate in an incorrect fashion. The reasons for this are many, but most commonly involve problems in distinguishing among the underlying cause of death, the immediate cause of death, the manner of death, and conditions contributing to death.[6]

Age is often associated with increase in major errors. Aging is often accompanied by the development of degenerative and chronic processes that affect many body systems. The question then arises as to which of the several co-existing conditions caused death. The clinician may logically say that none of the diseases singly, but rather a combination of conditions, caused the patient's death.[7] However it must be remembered that the attending physician is the one individual best able to prioritize the medical history in order to determine, in his or her best judgment, what disease process initiated the sequence of events leading to death.[6]

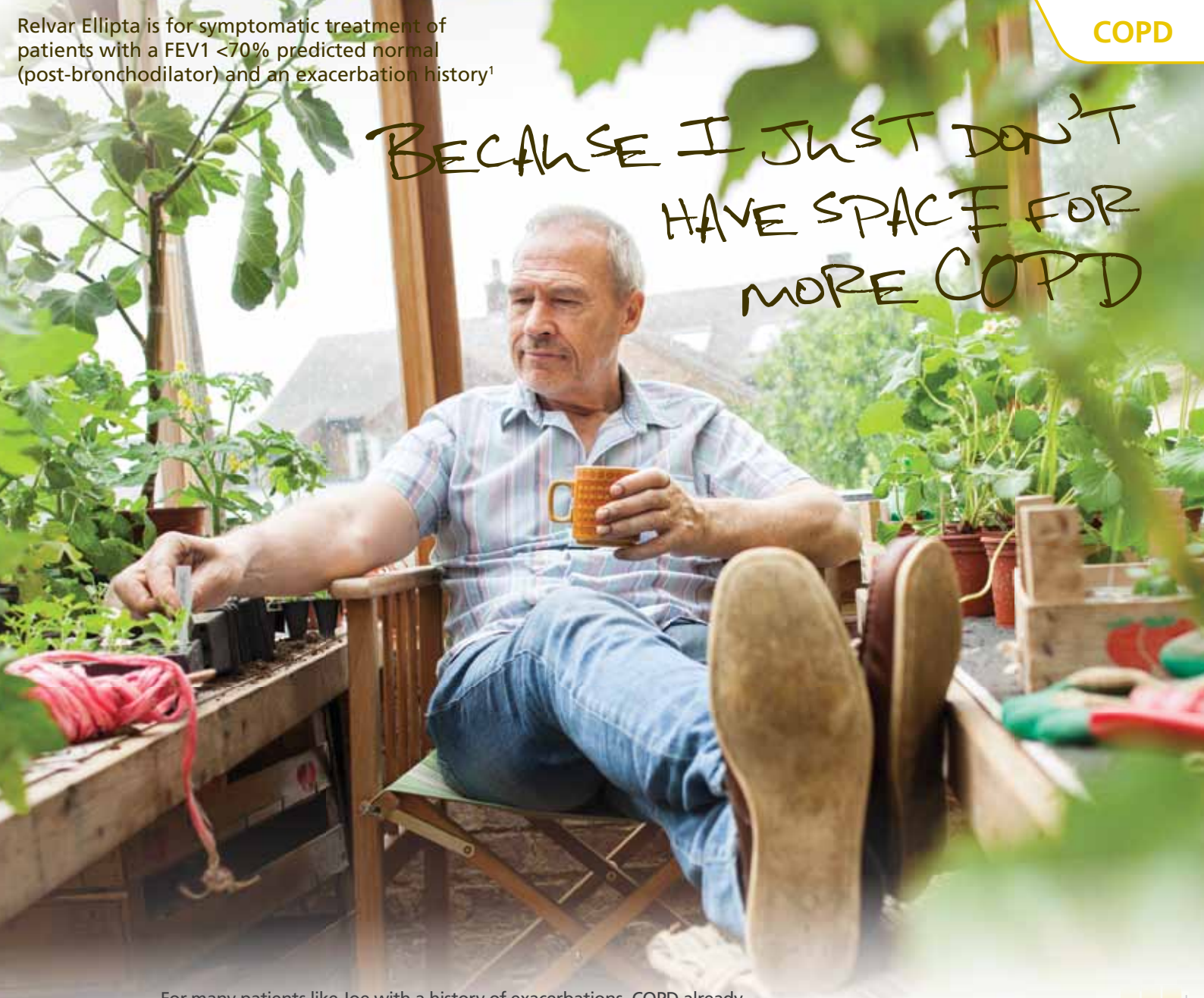
Doctors may find difficulty in completing a death certificate and distinguishing among the underlying cause of death, the immediate cause of death, the manner of death and conditions contributing to death. The increase in availability of electronic patient health data to doctors, especially general practitioners, is an important tool for reporting more specific information e.g. exact type of cancer.

While ad hoc training into the completion of the death certificate has been undertaken several times by the Directorate for Health Information and Research, death certificate completion is not included in any structured training programme for post-graduate doctors and new teaching tools need to be developed to reach as many doctors as possible in an on-going fashion.

REFERENCES CAN BE ACCESSED ON THESYNAPSE.NET

Relvar Ellipta is for symptomatic treatment of patients with a FEV1 <70% predicted normal (post-bronchodilator) and an exacerbation history[1]

COPD



For many patients like Joe with a history of exacerbations, COPD already takes up too much space in their life, yet they fear losing even more. So, when they need maintenance therapy, choose new Relvar Ellipta:

- The first ICS/LABA combination to deliver continuous 24-hour efficacy[2]
- In a practical, once-daily dose[1]
- Delivered in an easy to use device that patients prefer to their current inhaler[3,4*]

RELVAR® ELLIPTA®

(fluticasone furoate and vilanterol inhalation powder)

Practical efficacy

Relvar Ellipta (fluticasone furoate/vilanterol) Abridged Prescribing Information

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 on SPC how to report adverse reactions.

Please refer to the full Summary of Product Characteristics before prescribing

Trade Name: RELVAR ELLIPTA. **Active Ingredients:** 92 micrograms or 184 micrograms of fluticasone furoate and 22 micrograms of vilanterol (as trifenatate). **Pharmaceutical Form:** 92 micrograms/22 micrograms or 184 micrograms/22 micrograms inhalation powder, pre-dispensed. **Indications:** *The 92 micrograms/22 micrograms dose:* for the regular treatment of asthma in adults and adolescents aged 12 years and older where use of a combination medicinal product (long-acting beta$_2$-agonist and inhaled corticosteroid) is appropriate; and for the symptomatic treatment of adults with COPD with a FEV$_1$<70% predicted normal (post-bronchodilator) with an exacerbation history despite regular bronchodilator therapy. *The 184 micrograms/22 micrograms dose:* for the regular treatment of asthma in adults and adolescents aged 12 years and older where use of a combination medicinal product (long-acting beta$_2$-agonist and inhaled corticosteroid) is appropriate. **Dosage and Method of Administration:** *For Athsma:* One inhalation of Relvar Ellipta 92/22 micrograms or 184/22 micrograms once daily. Patients usually experience an improvement in lung function within 15 minutes of inhaling Relvar Ellipta. However, the patient should be informed that regular daily usage is necessary to maintain control of asthma symptoms and that use should be continued even when asymptomatic. If symptoms arise in the period between doses, an inhaled, short-acting beta$_2$-agonist should be taken for immediate relief. A starting dose of Relvar Ellipta 92/22 micrograms should be considered for adults and adolescents 12 years and over who require a low to mid dose of inhaled corticosteroid in combination with a long-acting beta$_2$-agonist. If patients are inadequately controlled on Relvar Ellipta 92/22 micrograms, the dose can be increased to 184/22 micrograms, which may provide additional improvement in asthma control. *For COPD:* One inhalation of Relvar Ellipta 92/22 micrograms once daily. Relvar Ellipta 184/22 micrograms is not indicated for patients with COPD. Relvar Ellipta is for inhalation use only. It should be administered at the same time of the day, each day. **Contraindications:** *Hypersensitivity* to the active ingredient or excipients. **Precautions for Use:** Fluticasone furoate/vilanterol should not be used to treat acute asthma symptoms, for which a short-acting bronchodilator is required. Caution in severe cardiovascular disease, moderate-to-severe hepatic impairment, pulmonary tuberculosis or in patients with chronic or untreated infections, history of diabetes mellitus and for paradoxical bronchospasm and pneumonia in patients with COPD. **Drug Interactions:** Beta-blockers, CYP3A4 inhibitors, P-glycoprotein inhibitors and sympathomimetic medicinal products (refer to the full Summary of Product Characteristics for list of drugs). **Fertility, Pregnancy and Lactation:** ***Pregnancy:*** No adequate data available. ***Lactation:*** insufficient information available. ***Fertility:*** There is no data in humans. Animal studies indicate no effect on fertility. **Effect on Ability to Drive or Use Machines:** No or negligible influence. **Undesirable Effects:** Very common side effects include headache and nasopharyngitis (refer to the full Summary of Product Characteristics for complete list of undesirable effects). **Overdose:** There is no specific antidote. Treatment of overdose should consist of general supportive measures. **Local Presentations:** Relvar Ellipta 92 micrograms/22 micrograms inhalation powder, pre-dispensed and Relvar Ellipta 184 *micrograms/ 22 micrograms inhalation powder, pre-dispensed*. **Legal Category:** POM. **Marketing Authorisation Holder:** Glaxo Group Limited, 980 Great West Road, Brentford, Middlesex TW8 9GS, United Kingdom **Marketing Authorisation Numbers:** EU/1/13/886/001-6 **DATE OF PREPARATION:** December 2013

In order to ensure that this product information reflects the mos up-to-date clinical and post-marketing surveillance data, please always refer to the latest Summary of Product Characteristics (SPC) which is available from GlaxoSmithKline (Malta) Ltd (Tel: +356 21238131)

REPORTING ADVERSE EVENTS (AEs):

Malta & Gibraltar: **If you become aware of any AEs, medication errors and/or use during pregnancy in association with GSK products, please report the event promptly to:** GSK (Malta) Limited, 1, De la Cruz Avenue, Qormi QRM 2458, Malta (Tel: +356 21238131)

Malta: **alternatively, any suspected AEs and medication errors can also be reported via the national Adverse Drug Reactions (ADRs) reporting system**

Report forms can be downloaded from www.medicinesauthority.gov.mt/adrportal and posted to the Malta Medicines Authority, Post-licensing Directorate, 203, Level 3, Rue D'Argens, Gżira GŻR 1368, MALTA, or sent by email to postlicensing.medicinesauthority@gov.mt

Gibraltar: **alternatively, any suspected AEs and medication errors can also be reported via the UK regulatory authority (MHRA):** https://yellowcard.mhra.gov.uk/

*Patients' current or previous maintenance inhalers: HandiHaler/ DISKUS/ MDI/ HFA (COPD); DISKUS/ MDI/ HFA (asthma).[4]

References: 1. Relvar Ellipta Summary of Product Characteristics. GlaxoSmithKline; 2013. **2.** Bleecker ER *et al.* Fluticasone furoate/vilanterol 100/25mcg compared with fluticasone furoate 100mcg in asthma: a randomized trial. *JACI In Practice* 2013 (in press). **3.** Svedstater H *et al.* Ease of use of a two-strip dry powder inhaler (DPI) to deliver fluticasone furoate/vilanterol (FF/VI) and FF alone in asthma. ERS. 2013. **4.** Woepse M *et al.* Qualitative assessment of a two-strip dry powder inhaler (ELLIPTA™) for COPD and asthma. EAACI. 2013.

MLT_GIB/RESP/0007/14 Date of preparation: January 2014

gsk

Theravance

Augmentin® SR

1000 mg/62,5 mg

Amoxicillin/Clavulanic Acid

Prolonged release tablets

- ✓ Unique bilayer tablet with immediate and sustained release delivery of amoxicillin provides superior efficacy against resistant pathogens[1,2]
- ✓ Recommended by leading Guidelines in the treatment of Community Acquired Pneumonia[3,4]
- ✓ Most common adverse effects are diarrhoea, nausea, vomiting and mucocutaneous candidiasis[5]
- ✓ Indicated for use in adults & adolescents aged ≥16 years; 2 tablets BD for 7-10 days[5]

Spreading infectious liveliness!

Mini Abridged Prescribing Information: *Please refer to full Summary of Product Characteristics (SPC) before prescribing.* **TRADE NAME:** Augmentin SR. **ACTIVE INGREDIENTS:** Amoxicillin (as trihydrate) and potassium clavulanate. **PRESENTATION:** 1000 mg/62.5 mg prolonged-release tablets. Supplied in 28 tablet packs. **INDICATION**: Treatment of community acquired pneumonia in adults and adolescents aged at least 16 years, caused or thought likely to be caused by penicillin-resistant *Streptococcus pneumoniae.* **POSOLOGY & ADMINISTRATION:** Oral use. Recommended dose of two tablets twice daily for seven to ten days. To minimise potential gastrointestinal intolerance, administer at the start of a meal. **CONTRAINDICATIONS:** Hypersensitivity (and past history of) to the active substances, to any penicillins or to any of the excipients. **SPECIAL WARNINGS & PRECAUTIONS:** Before initiating therapy careful enquiry of previous hypersensitivity reactions to beta-lactams. Where an infection is proven to be due to an amoxicillin susceptible organism, a switch to an amoxicillin-only preparation should be considered. Convulsions may occur in patients receiving high doses or who have impaired renal function. Concomitant use of allopurinol increase likelihood of allergic skin reactions. Prolonged use may occasionally result in overgrowth of non-susceptible organisms. Contains 29.3 mg (1.3 mmol) of sodium per tablet. *Refer to SPC's for full list of precautions.* **INTERACTIONS:** Penicillins may reduce the excretion of methotrexate causing a potential increase in toxicity. Concomitant use of probenecid is not recommended. If co-administration with oral anticoagulants is necessary, the prothrombin time or international normalised ratio should be carefully monitored with the addition or withdrawal of amoxicillin. Moreover, adjustments in the dose of oral anticoagulants may be necessary. Clinical monitoring should be performed during the combination with mycophenolate mofetil and shortly after antibiotic treatment. **PREGNANCY & LACTATION:** Use should be avoided unless considered essential by the physician. **UNDESIRABLE EFFECTS:** Very common (≥1/10): diarrhoea. Common (≥1/100, <1/10): mucocutaneous candidosis, nausea, abdominal pain. *Refer to SPC's for full list of undesirable effects*. **AUTHORISATION NUMBER:** AA 1051/00102. **MARKETING AUTHORISATION HOLDER:** GlaxoSmithKline Bulgaria EOOD. **LEGAL CATEGORY:** POM. **DATE OF PREPARATION:** July 2014. **In order to ensure that this product information reflects the most up-to-date clinical and post-marketing surveillance data, please always refer to the latest Summary of Product Characteristics (SPC) which is available from GlaxoSmithKline (Malta) Ltd (Tel: +356 21238131).** ***REPORTING ADVERSE EVENTS (AEs):*** **If you become aware of any AEs, medication errors and/or use during pregnancy in association with GSK products, please report the event promptly to:** GSK (Malta) Limited, 1, De la Cruz Avenue, Qormi QRM 2458, Malta (Tel: +356 21238131). **Alternatively, any suspected AEs and medication errors can also be reported via the national Adverse Drug Reactions (ADRs) reporting system:** Report forms can be downloaded from www.medicinesauthority.gov.mt/adrportal and posted to the Malta Medicines Authority, Post-licensing Directorate, 203, Level 3, Rue D'Argens, Gżira GŻR 1368, MALTA, or sent by email to postlicensing.medicinesauthority@gov.mt.

References:

1. Benninger MS. Amoxicillin/clavulanate potassium extended release tablets: a new antimicrobial for the treatment of acute bacterial sinusitis and community-acquired pneumonia. Expert Opin Pharmacother. 2003 Oct; 4(10): 1839-46.
2. Anthony R. White *et al.* Augmentin® (amoxicillin/clavulanate) in the treatment of community-acquired respiratory tract infection: a review of the continuing development of an innovative antimicrobial agent Journal of Antimicrobial Chemotherapy (2004) 53, Suppl. S1, i3–i20.
3. Gilbert DN, *et al.* Sanford guide to Antimicrobial Therapy v.3.11–last updated March 11, 2014. Sperryville; Antimicrobial Therapy, Inc. 2014 .
4. Mandell LA, Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. Clin Infect Dis. 2007 Mar 1; 44 Suppl 2: S27-72.
5. Augmentin SR SPC, April 2015.

Prepared: September 2015
Job No: MLT_GIB/AES/0002/15(2)

RENITA BUSUTTIL

MPSA

September was a very active month for MPSA members. A series of health campaigns were organised aimed at bringing the pharmacist closer to the public.

From the 19th until the 25th of September, MPSA celebrated World Pharmacists' Week in collaboration with the Department of Pharmacy, during which we visited various markets, namely Birgu, Birkirkara, Zurrieq, Valletta and Zabbar. During these visits we had the opportunity to meet the Minister for Social Dialogue, Consumer Affairs & Civil Liberties, Dr Helena Dalli. Free blood glucose and blood pressure tests were offered to the public, enabling the people to be more conscious about their state of health and highlighting the importance of regular check-ups. A questionnaire regarding the use of generic medicines was also distributed so as to gain an insight to the knowledge the general public has on the use of generic medicines, as well as to create awareness about the latter.

MPSA then worked hand in hand with the Chamber of Pharmacists (*Kamra Spiżjara*) to bring to the public an informative, yet entertaining night full of activities at Science in the City, which has become part of the Maltese events calendar. Science in the City is a yearly event, taking place on the 25th of September in Valletta, attracting thousands of families and tourists. This year our main objective was to emphasize the importance and use of prescriptions - delivered to the public through a small sketch between a pharmacist & a patient, depicting a scene from the daily encounters of a pharmacist. This was also accompanied by a short song interpreted by all students in which all the public engaged in. In addition, throughout the night we carried health checks, a quiz for children regarding healthy eating, informative sessions about osteoporosis and an interactive live molecule building. We cannot leave out our historic corner, which took us a step back in time to the ancient practice of medicine; and last but not least our mascot "Pirmlinu l-Pingwinu" who interacted with children, increasing their interest in our profession.

Both events were highly successful, receiving an overall positive response from the public. These were also a great opportunity for all students to gain exposure, interact with the public and practise daily tasks performed in a pharmacy.

59% of children wake at night due to their asthma[1]

Seretide® Evohaler®
50 mcg from 4 years[3]

Poppy is **50%** less likely to wake at night when using Seretide compared to baseline[2]

Seretide® Diskus®
100 mcg from 4 years[4]

Help Poppy by prescribing Seretide

Seretide is the only ICS/LABA proven to achieve guideline-defined asthma control in children[2]

Safety Information

Very common side effects: Headache and nasopharyngitis.
Common side effects: Candidiasis of mouth and throat, pneumonia, bronchitis, hypokalaemia and hoarseness/dysphonia
Special warnings and precautions for use: Systemic effects may occur with any inhaled corticosteroid, particularly at high doses prescribed for long periods. These effects are much less likely to occur than with oral corticosteroids.
It is important that patients are reviewed regularly and the dose of inhaled corticosteroid is reduced to the lowest dose at which effective control of asthma is maintained. Monitor height of children on prolonged inhaled steroid therapy.

Seretide™ (salmeterol xinafoate and fluticasone propionate)
Kindly refer to full Summary of Product Characteristics (SPC) before prescribing.
Abridged prescribing information. Presentations: For Malta and Gibraltar: *Seretide Diskus* – Each dose provides 50 microgram salmeterol xinafoate and 100 microgram, 250 microgram or 500 microgram respectively of fluticasone propionate. *Seretide 50 Evohaler* - Each dose provides 25 microgram salmeterol xinafoate and 50 microgram of fluticasone propionate. For Gibraltar only: *Seretide 125, 250 Evohaler:* Each dose provides 25 microgram salmeterol xinafoate and 125 microgram or 250 microgram of fluticasone propionate. **Therapeutic Indications:** For Malta and Gibraltar: *Seretide Diskus and Evohaler:* is indicated in the regular treatment of asthma where use of a combination (long-acting beta-2-agonist and inhaled corticosteroid) is appropriate. *Seretide Diskus* is indicated for the symptomatic treatment of patients with COPD with a FEV_1<60% predicted normal (pre-bronchodilator) and a history of repeated exacerbations, who have significant symptoms despite regular bronchodilator therapy. *Seretide 50 Evohaler* is used in patients not adequately controlled with inhaled corticosteroids and 'as needed' inhaled short acting beta-2-agonist or patients already adequately controlled on both inhaled corticosteroid and long-acting beta-2-agonist. For Gibraltar only: *Seretide 125, 250 Evohaler*: is indicated in the regular treatment of asthma where use of a combination (long-acting beta-2-agonist and inhaled corticosteroid) is appropriate. Used in patients not adequately controlled with inhaled corticosteroids and 'as needed' inhaled short acting beta-2-agonist or patients already adequately controlled on both inhaled corticosteroid and long-acting beta-2-agonist. **Dosage and administration:** Seretide is for inhalation use only. ***Seretide Diskus:*** Asthma – Adults and adolescents 12 years and over: one puff twice daily of Seretide 100 or Seretide 250 or Seretide 500 (each containing 50 mcg of salmeterol xinafoate and 100 mcg, 250 mcg or 500 mcg respectively of fluticasone propionate). Patients should be given the strength of Seretide containing the appropriate, lowest fluticasone propionate dosage for the severity of their disease. A short term trial of Seretide may be considered as initial maintenance therapy in adults or adolescents with moderate persistent asthma (defined as patients with daily symptoms, daily rescue use and moderate to severe airflow limitation) for whom rapid control of asthma is essential. In these cases, the recommended initial dose is one inhalation of 50 micrograms salmeterol and 100 micrograms fluticasone propionate twice daily. Once control of asthma is attained treatment should be reviewed and consideration given as to whether patients should be stepped down to an inhaled corticosteroid alone. Regular review of patients as treatment is stepped down is important. Seretide is not intended for the initial management of mild asthma. Seretide 50/100 micrograms strength is not appropriate in adults and children with severe asthma. Children 4-11 years: Seretide 100 Diskus (50 mcg salmeterol and 100 mcg fluticasone propionate) – one puff twice daily. ***Seretide Diskus:*** COPD: Seretide 500 Diskus (50 mcg of salmeterol xinafoate and 500 mcg fluticasone propionate) – one puff twice daily. ***Seretide 50 Evohaler:*** Adults and children 4 years and older: Two inhalations twice daily. For Gibraltar only: ***Seretide 125, 250 Evohaler:*** Adults and adolescents 12 years and older: Two inhalations twice daily. **Contra-indications:** Hypersensitivity. **Warnings and Precautions:** Seretide should not be used to treat acute asthma symptoms for which a fast- and short-acting bronchodilator is required. Patients should not be initiated on Seretide during an exacerbation, or if they have significantly worsening or acutely deteriorating asthma. Serious asthma-related events and exacerbations can occur during Seretide therapy; sudden and progressive deterioration in control or increased use of bronchodilator therapy warrants urgent medical assessment especially in patients of African-American origin (SMART). As with all inhaled medication containing corticosteroids, Seretide should be administered with caution in patients with pulmonary tuberculosis, severe cardiovascular disorders, including heart rhythm abnormalities, diabetes mellitus, untreated hypokalaemia/patients predisposed to hypokalaemia or thyrotoxicosis. In case of paradoxical bronchospasm discontinue Seretide, assess patient and give alternative therapy if necessary. Systemic effects may occur with any inhaled corticosteroid, particularly at high doses prescribed for long periods, but are less likely than with oral steroids. It is important, therefore, that the patient is reviewed regularly and the dose of inhaled corticosteroid is reduced to the lowest dose at which effective control of asthma is maintained. Prolonged treatment of patients with high doses of inhaled corticosteroids may result in adrenal suppression and acute adrenal crises. Rarely, a range of psychological or behavioural effects such as psychomotor hyperactivity, sleep disorders, anxiety, depression or aggression (particularly in children) may develop on prolonged use. Monitor height of children on prolonged inhaled steroid therapy. Transfer from oral steroids: Special care needed. Monitor adrenal function. Consider appropriate steroid therapy during periods of stress or elective surgery. Ritonavir can greatly increase the concentration of fluticasone propionate in plasma, therefore avoid concomitant use. There is also an increased risk of systemic side effects with other potent CYP3A inhibitors. There was an increased reporting of lower respiratory tract infections (particularly pneumonia and bronchitis) in the TORCH study in patients with COPD receiving Seretide compared with placebo; older patients, patients with a lower body mass index (<25kg/m^2) and patients with very severe disease (FEV_1<30% predicted) were at greatest risk of developing pneumonia regardless of treatment. Concomitant use of systemic ketoconazole significantly increases systemic exposure to salmeterol. This may lead to an increase in the incidence of systemic effects (e.g. prolongation in the QTc interval and palpitations). Concomitant treatment with ketoconazole or other potent CYP3A4 inhibitors should therefore be avoided unless the benefits outweigh the potentially increased risk of systemic side effects of salmeterol treatment. **Drug Interactions:** Avoid beta-blockers. Concomitant use with other beta-adrenergic containing drugs can have a potentially additive effect. Potent CYP3A4 inhibitors: Co-administration of ketoconazole (400 mg orally once daily) and salmeterol (50 mcg inhaled twice daily) resulted in a significant increase in plasma salmeterol exposure which may lead to an increase in the incidence of other systemic effects of salmeterol treatment (e.g. prolongation of QTc interval and palpitations) compared with salmeterol or ketoconazole treatment alone. The concomitant administration of ketoconazole should be avoided, unless the benefits outweigh the potentially increased risk of systemic side effects of salmeterol treatment. There is likely to be a similar risk of interaction with other potent CYP3A4 inhibitors (e.g. itraconazole, telithromycin, ritonavir). **Pregnancy and Lactation:** Experience limited. Balance risks against benefits. **Undesirable effects:** *Very Common/Common* - candidiasis of mouth and throat, pneumonia, bronchitis, hypokalaemia, headache, hoarseness/dysphonia, throat irritation (uncommon with Seretide 50 Evohaler), nasopharyngitis, sinusitis, contusions, traumatic fractures, arthralgia and myalgia, muscle cramps (uncommon with Seretide 50 Evohaler). See SPC for information on all adverse events. **Overdose:** *due to Salmeterol*: tremor, headache, tachycardia; *due to Fluticasone propionate:* temporary adrenal suppression.
MA Holder (Malta): GlaxoSmithKline (Ireland) Ltd. Trading as: Allen & Hanburys Ltd. **MA Numbers (Malta):** *Seretide Diskus:* MA 192/00901-3; *Seretide 50 Evohaler:* AA 192/00904. **Legal category**: POM. Not all pack sizes may be marketed. Date of revision of text: August 2013.

In order to ensure that this product information reflects the most up-to-date clinical and post-marketing surveillance data, please always refer to the latest Summary of Product Characteristics which is available from GlaxoSmithKline (Malta) Ltd (Tel: +356 21238131)

REPORTING ADVERSE EVENTS (AEs):
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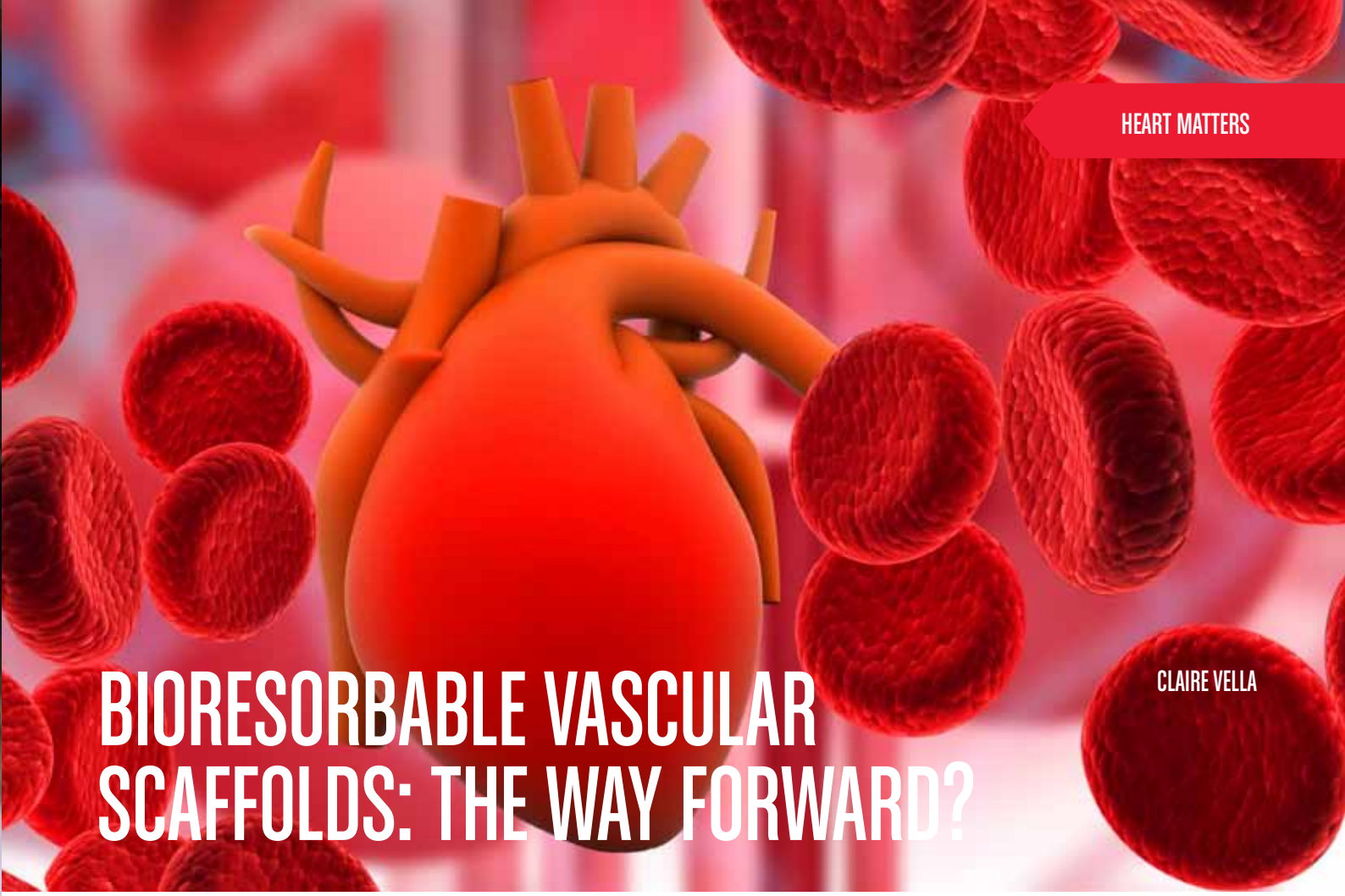
Malta: any suspected AEs and medication errors can also be reported via the national Adverse Drug Reactions (ADRs) reporting system:
Report forms can be downloaded from www.medicinesauthority.gov.mt/adrportal and posted to the Malta Medicines Authority, Post-licensing Directorate, 203, Level 3, Rue D'Argens, Gżira GŻR 1368, MALTA, or sent by email to postlicensing.medicinesauthority@gov.mt
Gibraltar: any suspected AEs and medication errors can also be reported via the UK regulatory authority (MHRA): https://yellowcard.mhra.gov.uk/

References
1. Wildhaber, J *et al. Pediatr. Pulmonol* 2012; 47:346–357.
2. DeBlic J *et al. Pediatr Allergy Immunol* 2009: 20:763–771
3. Seretide Evohaler (fluticasone propionate/salmeterol xinafoate) Summary of Product Characteristics, Allen & Hanburys Ltd. October 2014.
4. Seretide Accuhaler (fluticasone propionate/salmeterol xinafoate) Summary of Product Characteristics, Allen & Hanburys Ltd. October 2014.

Date of Preparation: **January 2015** ZINC CODE: **MLT_GIB/SFC/0002/15**

SERETIDE®
salmeterol/fluticasone propionate



BIORESORBABLE VASCULAR SCAFFOLDS: THE WAY FORWARD?

CLAIRE VELLA

With the sheer breadth of emerging evidence in the field, cardiology is remarkable in its ability to evolve and grow. The Malta Cardiac Society Conference in October 2015 discussed many advances in the specialty, but especially exciting was the announcement of the introduction of bioresorbable vascular scaffolds during percutaneous coronary interventions (PCI) carried out in Malta.

THE STORY SO FAR

When the advent of balloon angioplasty revolutionized treatment for coronary artery disease in 1977, patients who could previously only be treated with bypass surgery began to enjoy decreased morbidity and mortality rates. However, balloon angioplasty had significant early and late restenosis risk[1] which limited its long-term benefit. This led to the development of bare-metal stenting, which improved early failure rates but did not result in comparative improvement in long-term restenosis rates.[2]

Drug-eluting stents (DES) were a big step forward in terms of late restenosis risk. The landmark RAVEL study in 2002 showed significantly lower late luminal loss in sirolimus-coated stents compared to bare-metal stents, with a major cardiac adverse event (MACE) rate of 5.8% in the drug-eluting stent group compared to 28.8% in the bare-metal stent group.[3]

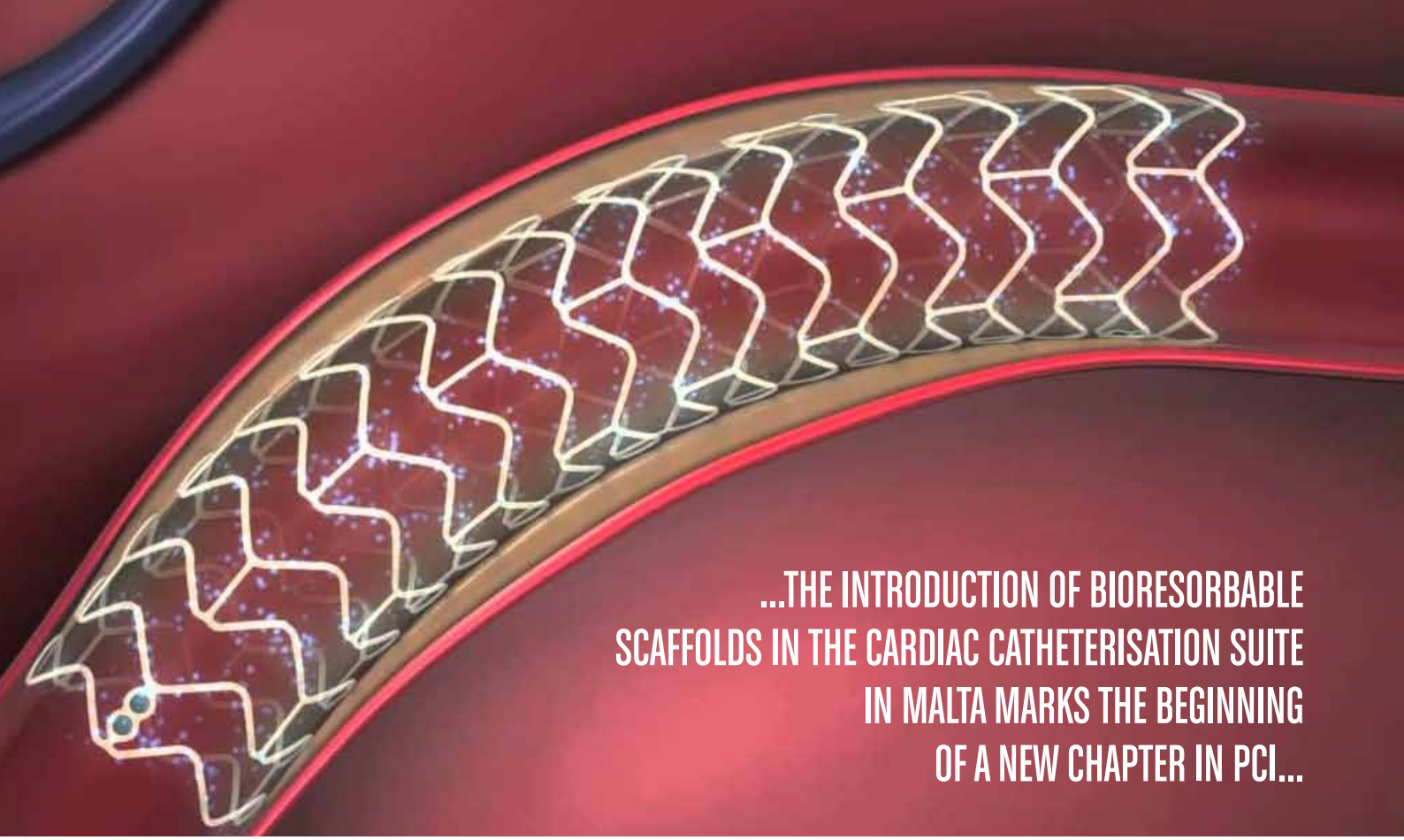
However, DES have been fraught with difficulties that belie their initial reception as life-saving for patients with coronary artery disease. Their comparatively rigid metal design has been shown to alter normal coronary flow dynamics due to impaired vasoconstriction. Moreover, the exposed metal framework in incompletely endothelialised stents is thought to lead to chronic inflammation which in turn leads to more delayed restenosis rates, with 10% needing repeat revascularization at 5 years.[4]

THE NEW KIDS ON THE BLOCK

Bioresorbable vascular scaffolds (BVSs) were born out of a need for better reperfusion techniques. Most models are made out of a flexible braided mesh of poly-L-lactic acid polymer (PLLA) or bioresorbable metal alloys coated with everolimus, and are reabsorbed completely within 5 years after deployment.[5]

The temporary nature of scaffolds is thought to confer a significant advantage in terms of restenosis rates as scaffolds are designed to be completely endothelialised before dissolving, leading to reduced local inflammation and restenosis while the artery slowly heals. The ABSORB-STEMI TROFI II clinical trial, published in September 2015, compared 6-month healing response rates between DES and BVS in patients undergoing primary PCI in ST-elevation myocardial infarction. Results showed that there was no difference in arterial healing between both groups at 6 months, proving non-inferiority of bioresorbable scaffolds in this regard.[6]

Moreover, the ABSORB-III clinical trial is currently underway, designed to prove superiority of BVS compared to conventional everolimus-eluting metal stents in elective PCIs for stable and unstable myocardial ischemia.[7] This large-scale,



...THE INTRODUCTION OF BIORESORBABLE SCAFFOLDS IN THE CARDIAC CATHETERISATION SUITE IN MALTA MARKS THE BEGINNING OF A NEW CHAPTER IN PCI...

multicenter randomized trial aims to determine the difference between BVS and DES groups with a primary endpoint of target lesion failure, defined as restenosis, myocardial infarction in the relevant territory, and cardiac death. The first results are expected next year, but are expected to show optimistic findings with respect to BVS.

BVS AND ANTIPLATELET THERAPY

The use of dual antiplatelet therapy with aspirin and a P2Y12-receptor inhibitors, such as clopidogrel and prasugrel, has long gone hand in hand with cardiac stenting in order to prevent restenosis. With the finite lifespan of scaffolds, one could postulate that antiplatelet therapy may possibly be stopped at an earlier stage, especially in patients with high bleeding risk.

However, even with their short lifespan and superior endothelialisation, there is still a risk of thrombosis with scaffolds, especially if they have not been properly implanted.[8] Furthermore, early discontinuation or absence of antiplatelet therapy has been shown to be associated with scaffold thrombosis.

The current consensus is that at least 6-12 months of dual antiplatelet therapy are needed after BVS insertion,[9] followed by lifelong aspirin. However, the kind of device used together with patient preference and bleeding risk play an important role in choice of therapy.[10]

LIMITATIONS AND GAPS IN EVIDENCE

While BVS is being touted in some circles as the future of PCI, the reality is that the technology is far too young for us to really tell what will happen. Even though evidence is slowly starting to mount and the picture is becoming clearer with respect to short- and long-term advantages and disadvantages of the devices, there are still lacunae in our knowledge.

An obvious presumed limitation is the use of more fragile scaffolds in tough, calcified arteries as opposed to metal stents – evidence regarding efficacy in this regard is particularly limited.

There is also a lack of large studies on outcomes in patients who need repeated PCI. Scaffolds would in theory lend themselves better to situations where repeat revascularization is needed, avoiding the "full metal jacket" that is unfortunately all too common in patients with uncontrolled ischaemic heart disease.

Although studies have mostly focused on the insertion of scaffolds in ST segment elevation MI and chronic ischaemic heart disease, patients with chronic total occlusion have mostly been sidelined. There are some small, single-centre studies that indicate that BVS shows promising results in chronic total occlusion,[11] but there is a glaring lack of robust multicenter randomized controlled trials.

THE WAY FORWARD

BVS are incredibly promising, but there appear to be limitations to their use. The 2014 European Society of Cardiology guidelines on Myocardial Revascularisation[12] do not give more than a brief overview about scaffolds and are cautious about indications for use, pending randomized controlled trials. Certainly, however, the introduction of bioresorbable scaffolds in the Cardiac Catheterisation Suite in Malta marks the beginning of a new chapter in PCI and as newer evidence emerges, we will see exactly where these novel devices fit in the bigger picture.

REFERENCES CAN BE ACCESSED ON THESYNAPSE.NET

Percarnil

Perindopril 4mg tablets
ACE Inhibitor Antihypertensive

For further information please refer to the full summary of product characteristics or to our website www.actavis.com.mt

Actavis

ACT 08.2013 - JPA37843

VICTOR GRECH

THE EYES AND VISION IN STAR TREK

"THEY SAY THE EYE IS THE WINDOW TO THE SOUL. IN THIS CASE IT'S A LITTLE BIT MORE"[1]

Eyesight and the eyes themselves are regularly employed in science fiction, not only as important motifs enjoying central roles in the plot, but also in other aspects of the story, such as in characterization. This article will review some interesting aspects of eyesight and of the visual organs as exploited by *Star Trek* (ST). In the canon, the eyes have been used for two main purposes: as signifiers of difference and otherness, that is, of alienness, and as a showcase for medical advances.

ST uses physical characteristics as signifiers for "the other." Common methods include subtle or even sophisticated make-up alterations to the head and face and other visible portions of the body. These may be simple changes, such as pigmented spots, or elaborate transformations that involve the face and cranium including monocular replacement with a wide variety of cybernetic implants in the Borg alien race. The latter famously give Captain Picard a spectacular nightmare when he dreams that he is being reassimilated by the Borg, and we witness a small drill bit gently indenting his cornea and stopped just short of going into his eye.[2]

Elasian females produce tears containing compounds that upon skin contact, enthral men and render them emotionally infatuated, such that "a man whose flesh is once touched by the tears of a woman of Elas has his heart enslaved forever".[3] The ultimate in ocular difference are the Aenar species who live in caves on a frozen world, "blind ice-dwellers" and this disability is made up for by highly-evolved telepathic abilities.[4]

Rituals involving the eyes may also function as a signifier for difference. For example, the Klingon warrior death ritual involves forcibly opening the warrior eyes during or directly after his death, then bellowing loudly skyward, warning the inhabitants of Sto-vo-kor (the afterlife for the honored dead, equivalent to the Norse Valhalla) that a warrior is about to arrive.[5] Blind alien animals are also mentioned in the canon, such as the Tiberian bat, and being called "as blind as a Tiberian bat" is considered a perjorative.[6]

Injury during the course of duty may also include blindness, temporarily or permanently creating a difference. For example, the Vulcan Spock is blinded by deliberate exposure to strong sunlight that is used to drive a parasite out of his nervous system but the blindness was temporary due to an inner eyelid.[7] Humans are less able to tolerate strong sunlight, such as that on the planet Vulcan;[8] however species who are accustomed to low light levels, such as the Myleans, have dilated pupils which lead to photophobia in relatively strong light intensities that are tolerated by humans.[9]

The Klingon general Martok lost one eye when he was forced to engage in recreational hand-to-hand combat, but being a typical hypermacho Klingon, spurns a replacement.[10] The Vulcan Tuvok was also blinded during an explosion but this is reversed when the timeline in which the events occur is erased, and it is as if he never experienced blindness. During his blind period, his work panel interface was modified to incorporate a tactile interface.[11] And finally, the Cardassian villain Dukat was temporarily blinded by an energy burst released from a Bajoran holy book.[12]

The eyes are routinely used as personal identifiers with biometric retinal scans.[13] More importantly, blindness has been greatly alleviated within the Federation. Early in the canon, blind individuals are able to function as normal members of society through a highly sophisticated sensor web worn on clothing.[14] Two centuries later, blind individuals take advantage of medical devices called VISORs (Visual Instrument and Sensory Organ Replacement), goggle-like structures which are able to detect electromagnetic signals between 1 Hz and 100,000 THz.[15]

Ocular implants were developed a few years later. These were similar in appearance to the human eye but were of a deep blue colour. Moreover, a close inspection reveals mechanized details on the iris and pupils. They offer additional advantages such as telescopic vision.[2] These devices may be implanted in individuals who are blind from birth[2], blinded by an injury, such as in battle,10 or after an eye has been explanted and replaced with a mechanical (such as a cybernetic Borg) interface.[1] Interestingly, normal vision is not always desirable since this would lead to a *reduction* in visual abilities.[16]

Ironically, the only extant implantation of an organic eye within the canon is that of Data, an android who is given an organic eye along with other organic implants in the Borg Queen's attempt to seduce him.[2]

The eyes are important organs and it is only fitting that they are important protagonists in ST. Even episode titles sometimes accede to this, and in particular, when there is anachronie which speed up in external narration when compared with events occurring on starships, the eyes are mentioned in the episode titles, such as when the *Enterprise* is invaded by speeded-up aliens[17] or when *Voyager* orbits a planet on which time flies by at an accelerated rate.[18]

ST portrays blindness as a curable disease, in the future, and even provides opportunities for vision enhancement with abilities superior to mundane vision in individuals with impaired sight.

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Dosage and Administration Asthma Not intended for the initial management of asthma. Dose should be individualised. If a patient requires dosages outside recommended regimen, appropriate doses using individual inhalers should be prescribed. When long-term symptoms are controlled, titrate to the lowest effective dose, which could include a once daily dosage. **Symbicort maintenance therapy – regular maintenance treatment with a separate rescue medication: *Adults* (≥18 years, *including elderly*):** 1-2 inhalations twice daily (maximum 4 inhalations twice daily). ***Adolescents (12-17 years):*** 1-2 inhalations twice daily. ***Children 6-11 years (Symbicort 100/6 only):*** 2 inhalations twice daily. ***Children under 6 years:*** Not recommended.
Symbicort maintenance and reliever therapy – regular maintenance treatment and as needed in response to symptoms: consider for patients with (i) inadequate asthma control and in frequent need of reliever medication (ii) previous asthma exacerbations requiring medical intervention. ***Adults (including elderly):*** 1 inhalation twice daily or as 2 inhalations once daily. 2 inhalations twice daily may be appropriate for some patients (200/6 strength only). Patients should take 1 additional inhalation as needed in response to symptoms. If symptoms persist after a few minutes, an additional inhalation should be taken. Not more than 8 inhalations should be taken on any single occasion. A total daily dose of more than 8 inhalations is not normally needed; however, up to 12 inhalations a day could be used for a limited period. Patients using more than 8 inhalations daily should be strongly recommended to seek medical advice and should be reassessed; their maintenance therapy should be reconsidered. Patients should be advised to always have Symbicort for reliever use. ***Children and adolescents under 18 years of age:*** not recommended. **COPD *(Symbicort 200/6 only): Adults (≥ 18 years):*** 2 inhalations twice daily.
Contraindications Hypersensitivity to active substances or excipient.
Warnings and Precautions If treatment is ineffective, or exceeds the highest recommended dose therapy should be reassessed. Sudden and progressive deterioration in control requires urgent medical assessment. Treatment should not be stopped abruptly. Patients should have their appropriate rescue medication available at all times i.e. either Symbicort or a separate reliever. If needed before exercise a separate reliever should be used. Therapy should not be initiated during an exacerbation. Serious asthma-related adverse events and exacerbations may occur. If asthma symptoms remain uncontrolled or worsen patients should continue treatment but seek medical advice. If paradoxical bronchospasm occurs Symbicort should be discontinued. It responds to a rapid-acting inhaled bronchodilator and should be treated straightaway. Systemic effects may occur, particularly at high doses prescribed for long periods e.g. Cushing's syndrome, Cushingoid features, adrenal suppression, growth retardation in children and adolescents, cataract, glaucoma and more rarely a range of psychological or behavioural effects including psychomotor hyperactivity, sleep disorders, anxiety, depression or aggression (particularly in children). Height of children should be monitored. Potential effects on bone should be considered especially in patients on high doses for prolonged periods that have co-existing risk factors for osteoporosis. Prolonged treatment with high doses of inhaled corticosteroids, particularly higher than recommended doses, may also result in clinically significant adrenal suppression. Additional systemic corticosteroid cover should be considered during periods of stress e.g. severe infections or elective surgery. Transfer from oral steroid therapy to Symbicort may result in the appearance of allergic or arthritic symptoms which will need treatment, in rare cases, tiredness, headache, nausea and vomiting can occur due to insufficient glucocorticosteroid effect and temporary increase in the dose of oral glucocorticosteroids may be necessary. To minimise risk of oropharyngeal candida infection patients should rinse mouth with water. Observe caution in patients with thyrotoxicosis, phaeochromocytoma, diabetes mellitus, untreated hypokalaemia, or severe cardiovascular disorders. Re-evaluate need for Symbicort in patients with active or quiescent pulmonary tuberculosis, fungal and viral infections in the airways. Hypokalaemia may occur at high doses. Particular caution recommended in unstable or acute severe asthma. Monitor serum potassium levels, in diabetic patients consider additional blood glucose monitoring. The small amounts of milk proteins present may cause allergic reactions.
Drug Interactions Concomitant treatment with potent CYP3A4 inhibitors should be avoided, if this is not possible the time interval between administration should be as long as possible. Symbicort maintenance and reliever therapy is not recommended in these patients. Not recommended with beta adrenergic blockers (including eye drops) unless compelling reasons. Concomitant administration with quinidine, disopyramide, procainamide, phenothiazines, antihistamines (terfenadine) and TCAs can prolong the QTc interval and increase the risk of ventricular arrhythmias. L-Dopa, L-thyroxine, oxytocin and alcohol can impair cardiac tolerance. Concomitant administration with MAOIs, including agents with similar properties such as furazolidone and procarbazine, may precipitate hypertension. Elevated risk of arrhythmias in patients receiving anaesthesia with halogenated hydrocarbons. Hypokalaemia may increase the disposition towards arrhythmias in patients taking digitalis glycosides
Fertility, Pregnancy and Lactation No data available on the potential effect on fertility. During pregnancy, use only when the benefits outweigh the potential risks. Budesonide is excreted in breast milk, however at therapeutic doses no effects on the child are anticipated.
Undesirable effects Common: headache, palpitations, tremor, Candida infections in the oropharynx, coughing, mild irritation in the throat, hoarseness. Uncommon: tachycardia, muscle cramps, nausea, dizziness, bruises, aggression, psychomotor hyperactivity, anxiety, sleep disorders. Rare: hypokalaemia, cardiac arrhythmias including atrial fibrillation, supraventricular tachycardia and extrasystoles, bronchospasm and immediate and delayed hypersensitivity reactions including exanthema, urticaria, pruritus, dermatitis, angioedema and anaphylactic reaction. Very Rare: depression, behavioural changes (predominantly in children), angina pectoris, prolongation of QTc-interval, hyperglycaemia, taste disturbance, Cushings syndrome, adrenal suppression, growth retardation, decrease in bone mineral density, cataract, glaucoma and variations in blood pressure. As with other inhalation therapy, paradoxical bronchospasm may occur in very rare cases.
Package Quantities Each Symbicort Turbohaler contains 120 inhalations. **Legal Status** POM. **Marketing Authorisation Numbers** MA 046/00001-2. **Marketing Authorisation Holder (MAH)** AstraZeneca AB, Gartunavagen, S-151 85 Sodertalje, Sweden. **Further product information available on request from** Associated Drug Company Limited, Triq l-Esportaturi, Mriehel, Birkirkara BKR 3000, Malta. Tel (+356) 2277 8115.
Abridged Prescribing Information prepared 12/14.
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References: 1. Adelphi Respiratory Disease Specific Programme 2006. **2.** Olof Selroos et al. *Treat Respir Med* 2006; 5 (5): 305-315. **3.** Engel et al. Br J Clin Pharmacol 1992; 33(4): 436-44.

ALBERT CILIA-VINCENTI

THE CHOLESTEROL CONTROVERSY – THE SERIES

In the previous instalment we learnt how Ronald Krauss, one of the most respected nutrition researchers, had worked out that LDL-cholesterol consisted of two sub-fractions, one with large soft particles and the other with small dense particles, and that the small dense particle sub-fraction was the one linked to atherosclerosis and not the other. He also noted that saturated fats increased the "good" sub-fraction and lowered the "bad" sub-fraction, and that carbohydrates did the opposite. This suggested that carbohydrates were implicated in atherosclerosis rather than saturated fat.

Krauss did not push his LDL sub-fraction findings too hard with his colleagues, even after they had been confirmed by others,[1] lest they might get very upset at the implication that they had been wrong about LDL-cholesterol all along. Indeed, most of his peers found it convenient to ignore his findings. However, in 1996 he managed to make the point in the American Heart Association's (AHA) guidelines that saturated fatty acids in diary, meat and palm oil were different and did not have the same effect on blood lipids.[2] It took another decade for other guidelines to incorporate these fine points about different saturated fats, and then only in France. The French 2010 official dietary advice noted that only saturated fats found predominantly in palm and coconut oil could possibly be linked to atherosclerosis due to their effect on LDL-cholesterol, and that the saturated fat found in meat, dairy and eggs was completely exonerated.

In the end, however, Krauss lost the battle to traditionalists, and in 2006 the AHA guidelines swung back from Krauss's recommendation to consume 8-10% of total calories from saturated fat.[3] In 2013, the American College of Cardiology (ACC), updating the coronary artery disease treatment recommendations, issued draconian advice – all "at risk" adults (some 45 million healthy people) were told, as a precautionary measure, to cut their saturated fat intake down to an unprecedented 5% to 6% of calories – approaching a vegan diet. This recommendation was justified quoting the DASH and OmniHeart studies, in which subjects were fed diets containing 5% to 6% saturated fat and their LDL-cholesterol levels dropped significantly.[4,5] This could be interpreted as a positive only if Krauss's work was ignored, along with other trials showing LDL wasn't a meaningful indicator of risk for most people. The ACC also had to ignore the fact that subjects in these two trials saw their HDL-cholesterol fall significantly (a bad indicator), that there was no improvement in their markers for diabetes, and that they lost no weight.

In making its very low saturated fat recommendations, the ACC stated it did not consider the impact of its proposed diet on diabetes or metabolic syndrome – a truly starling decision, given that these conditions are closely linked with atherosclerotic cardiovascular disease. Furthermore, the ACC guidelines ignored several decades' worth of large trials, including MRFIT and the Women's Health Initiative, which collectively tested more than 61,000 men and women for more than 7 years, and which failed to show any benefits of a low-saturated fat diet. Instead, the two trials quoted by ACC tested only 590 people over 8 weeks.

Moreover, the ACC continued to extrapolate that dietary LDL-lowering had the same biological significance as statin-induced LDL-lowering. There is no data to support this assumption, and the significance of LDL as a biomarker of heart attack risk is increasingly doubtful. Unfortunately, the AHA 2015 (updated 12th August) dietary guidelines have adopted the ACC's 5% to 6% saturated fat recommendation.

By ignoring all the diet and LDL-cholesterol evidence, including Krauss's LDL sub-fractions work, the AHA/ACC have preserved LDL as their favoured biomarker, as though the last 20 years of science have never happened. The rationale for their recommendations remains more political and financial than scientific. Indeed, LDL-cholesterol has a following and a long history; doctors understand it, governments have entire bureaucracies committed to lowering it, academics have invested their careers in it, and pharmaceutical companies have promoted it.

In a highly controversial move, the ACC 2013 guidelines did appear to downgrade LDL-cholesterol *slightly* by eliminating the specific numerical treatment targets which had been in place since 1986 (total cholesterol <5.17mmol/L; LDL <3.36 mmol/L; HDL >0.91mmol/L; fasting triglycerides 0.45–1.69mmol/L). They also promoted "non-HDL-cholesterol" as a new additional biomarker. This is calculated by subtracting HDL from total cholesterol but, like LDL, its accuracy significantly drops when triglycerides are high.

These changes seem to be in the right direction for understanding atherosclerosis, but forces separate from science may have been at work here too. A cynical observer might point to the statin drugs' patents which have expired in 2013 and that, as such, incentives for pharmaceutical companies to continue favouring LDL were therefore reduced.

Many diet and disease experts, including Krauss, are disappointed by the continued focus on LDL-cholesterol. When in 2006 the AHA guidelines undid all of Krauss's work on saturated fat, he is said to have become disenchanted with the dietary guideline process and ramped down his activity within the AHA. Indeed, in 2011, he gave up a coveted spot on its expert panel since he could not endorse the direction in which it was heading.

To be continued

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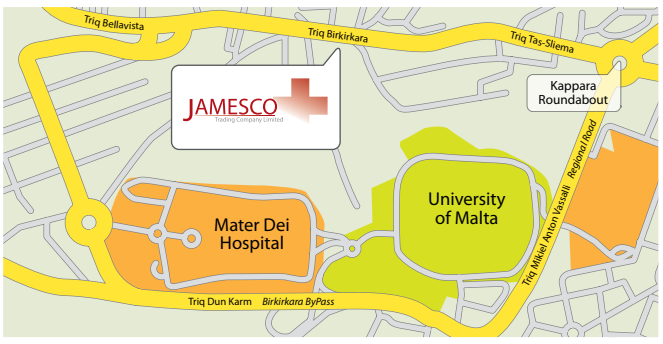

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MARIKA AZZOPARDI

TO ROMANIA & BACK

MARIA GALEA HAS RECENTLY GRADUATED AS PHARMACIST AND TALKS TO MARIKA AZZOPARDI ON HER RECENT TRAVELS

TS: HOW LONG HAVE YOU BEEN A PHARMACIST?

I finished my pharmacy course this summer and am going to graduate this December. I am working as a community pharmacist which I love. I consider my job as more than just a job ... I consider it as a vocation and my passion.

TS: YOU WERE IN ROMANIA THIS SUMMER, JUST BEFORE FINALISING YOUR STUDIES. HOW DID YOU END UP GOING TO ROMANIA?

I always wanted to do voluntary work but there never seemed to be the right time for it. When the opportunity for this voluntary experience came in the summer of 2014, I decided to take the plunge. After the wonderful experience of last year, the decision on whether I go again this summer was not so hard. Unfortunately I had to cut this year's experience by a week, due to unexpected thesis obligations.

TS: WHY ROMANIA?

I always knew that I would one day travel to a distant land on a voluntary mission but quite frankly never actually considered Romania. However, when I got to know of this experience being organized by a group of youths from the Naxxar Parish Church, I figured out that it was as good a place as any. It was pointless postponing any kind of voluntary experience till one had the time to do a longer experience or in a distant place.

TS: WHAT WERE THE PURPOSES OF THIS MISSION?

To raise funds to donate to the poor and needy, and to carry out mission work. We lived at a home of the Sisters of Mother Theresa in Chitila which is a short distance away from Bucharest. At this home the Sisters care for about 15 men who have severe disabilities, both mental and physical.

Maria Galea (bottom, second from right)

Maria Galea (third from right)

TS: WHAT WAS YOUR INITIAL REACTION WHEN YOU ARRIVED THERE?

Shock. In our communication before we went to Romania, the Sisters always referred to their residents as the boys'). However, when we arrived there, we realised that 'the boys' were actually adult men, aged 30 and over. Secondly, it is a culture shock having to take in a sudden change from our lifestyle to the kind of run-down village with its ensuing poverty and poor living conditions that is Chitila.

TS: HOW DID YOU SPEND YOUR DAYS?

We helped the Sisters. We carried out extensive maintenance work, painted rooms, refurbished a chapel, helped to care for the 'boys' and organised camps for the local children who are mostly Romanians. We also assisted the Brothers who gathered and fed the homeless and drug addicts at a local day centre.

TS: WHAT WERE THE GREATEST HURDLES YOU HAD TO OVERCOME ON A PERSONAL LEVEL?

Having to feed a disabled adult person, witnessing the lack of access to healthcare, as well as experiencing what was considered as the norm for the local children we met during the camps. The persons we met did not know English and we did not know Romanian. Not knowing the language, we resorted to using sign language, basic words, and just hugging when we couldn't understand what was happening. Then we had to settle at night with the screams and shouting coming from the quarters of the mentally disabled patients. However, the initial shock quickly passed and we grew to love the residents at the home. Leaving was hard, both for us and for the people we met there. The rift of separation became more evident upon arriving for our second visit. One of the patients actually ran out to greet us with open arms and great enthusiasm. He remembered us with warm feelings. Needless to say, it was hard to say goodbye again.

TS: WOULD YOU DO IT AGAIN?

Most certainly. Perhaps not in Romania, perhaps yes. I would like to experience other missions. Romania has taught me a lot about survival, self-reliance, the appreciation of a simple lifestyle - we didn't need our mobile phones or social media. You hear abominable stories of desertion and neglect but at the same time amaze yourself with the ensuing stories of survival, regardless of all obstacles. The children in Romania crave love. Our visit was only a drop in the ocean. We had to accept that as much as we wanted we could not change their life, however, in our small and humble way, we managed to give the people we met some joy and warmth at least for one day.

I READ THE SYNAPSE BECAUSE...

it is very interesting. Actually it is the most frequently published, local medical production, so it is a good way to keep myself updated

A JOKE A DAY KEEPS THE DENTIST AT BAY

A MAN WAS ARGUING WITH HIS NEIGHBOR AND FINALLY SAID, "I WILL GIVE YOU A PUNCH ON THE JAW SO HARD, THAT THE DENTIST WILL START SENDING ME HAMPERS FOR CHRISTMAS"...

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▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. Refer to section 4.8 of the SmPC for how to report adverse reactions. **PRESENTATION:** Each capsule contains 143 µg of indacaterol maleate equivalent to 110 µg of indacaterol and 63 µg of glycopyrronium bromide equivalent to 50 µg of glycopyrronium. Each delivered dose (the dose that leaves the mouthpiece of the inhaler) contains 110 µg of indacaterol maleate equivalent to 85 µg of indacaterol and 54 µg of glycopyrronium bromide equivalent to 43 µg of glycopyrronium. **INDICATIONS:** Ultibro Breezhaler is indicated as a maintenance bronchodilator treatment to relieve symptoms in adult patients with chronic obstructive pulmonary disease (COPD). **DOSAGE AND ADMINISTRATION:** The recommended dose is the inhalation of the content of one capsule once daily using the Ultibro Breezhaler inhaler. Ultibro Breezhaler is recommended to be administered at the same time of the day each day. If a dose is missed, it should be taken as soon as possible on the same day. Patients should be instructed not to take more than one dose in a day. Ultibro Breezhaler can be used at the recommended dose in elderly patients (75 years of age and older). Ultibro Breezhaler can be used at the recommended dose in patients with mild to moderate renal impairment. In patients with severe renal impairment or end-stage renal disease requiring dialysis it should be used only if the expected benefit outweighs the potential risk. Ultibro Breezhaler can be used at the recommended dose in patients with mild and moderate hepatic impairment. There are no data available for the use of Ultibro Breezhaler in patients with severe hepatic impairment, therefore caution should be observed in these patients. There is no relevant use of Ultibro Breezhaler in the paediatric population (under 18 years) in the indication COPD. The safety and efficacy of Ultibro Breezhaler in children have not been established. No data are available. Method of administration For inhalation use only. The capsules must not be swallowed. The capsules must be administered only using the Ultibro Breezhaler inhaler. Patients should be instructed on how to administer the product correctly. Patients who do not experience improvement in breathing should be asked if they are swallowing the medicine rather than inhaling it. **CONTRAINDICATIONS:** Hypersensitivity to the active substance or to any of the other excipients. **WARNINGS/PRECAUTIONS:** Ultibro Breezhaler should not be administered concomitantly with medicinal products containing other long acting beta adrenergic agonists or long acting muscarinic antagonists, the pharmacotherapeutic groups to which the components of Ultibro Breezhaler belong. Asthma: Ultibro Breezhaler should not be used for the treatment of asthma due to the absence of data in this indication. Long acting beta2 adrenergic agonists may increase the risk of asthma related serious adverse events, including asthma related deaths, when used for the treatment of asthma. Not for acute use: Ultibro Breezhaler is not indicated for the treatment of acute episodes of bronchospasm. Hypersensitivity related to indacaterol or glycopyrronium: Immediate hypersensitivity reactions have been reported after administration of indacaterol, one of the components of Ultibro Breezhaler. If signs suggesting allergic reactions (in particular, difficulties in breathing or swallowing, swelling of tongue, lips and face, urticaria, skin rash) occur, treatment should be discontinued immediately and alternative therapy instituted. ***Paradoxical bronchospasm:*** In clinical studies with Ultibro Breezhaler, paradoxical bronchospasm was not observed. However, paradoxical bronchospasm has been observed with other inhalation therapy and can be life threatening. If this occurs, treatment should be discontinued immediately and alternative therapy instituted. *Narrow-angle glaucoma:* No data are available in patients with narrow angle glaucoma, therefore Ultibro Breezhaler should be used with caution in these patients. Patients should be informed about the signs and symptoms of acute narrow angle glaucoma and should be informed to stop using Ultibro Breezhaler should any of these signs or symptoms develop. Urinary retention: No data are available in patients with urinary retention, therefore Ultibro Breezhaler should be used with caution in these patients. Patients with severe renal impairment: These patients should be monitored closely for potential adverse reactions. ***Cardiovascular effects:*** Ultibro Breezhaler should be used with caution in patients with cardiovascular disorders (coronary artery disease, acute myocardial infarction, cardiac arrhythmias, hypertension). ***Hypokalaemia:*** Beta2 adrenergic agonists may produce significant hypokalaemia in some patients, which has the potential to produce adverse cardiovascular effects. The decrease in serum potassium is usually transient, not requiring supplementation. In patients with severe COPD, hypokalaemia may be potentiated by hypoxia and concomitant treatment, which may increase the susceptibility to cardiac arrhythmias. Clinically relevant effects of hypokalaemia have not been observed in clinical studies of Ultibro Breezhaler at the recommended therapeutic dose. ***Hyperglycaemia*** Inhalation of high doses of beta2 adrenergic agonists may produce increases in plasma glucose. Upon initiation of treatment with Ultibro Breezhaler plasma glucose should be monitored more closely in diabetic patients. Ultibro Breezhaler should be used with caution in patients with convulsive disorders or thyrotoxicosis, and in patients who are unusually responsive to beta2 adrenergic agonists. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose galactose malabsorption should not take this medicine. ***Pregnancy and Lactation:*** There are no data from the use of Ultibro Breezhaler in pregnant women available. Indacaterol may inhibit labour due to a relaxant effect on uterine smooth muscle. Therefore, Ultibro Breezhaler should only be used during pregnancy if the expected benefit to the patient justifies the potential risk to the foetus. It is not known whether indacaterol, glycopyrronium and their metabolites are excreted in human milk. The use of Ultibro Breezhaler by breast feeding women should only be considered if the expected benefit to the woman is greater than any possible risk to the infant. **INTERACTIONS:** Information on the potential for interactions is based on the potential for each of its two components. Beta adrenergic blockers may weaken or antagonise the effect of beta2 adrenergic agonists. Therefore Ultibro Breezhaler should not be given together with beta-adrenergic blockers (including eye drops) unless there are compelling reasons for their use. Where required, cardioselective beta adrenergic blockers should be preferred, although they should be administered with caution. The co administration of Ultibro Breezhaler with other anticholinergic containing medicinal products has not been studied and is therefore not recommended. Concomitant administration of other sympathomimetic agents (alone or as part of combination therapy) may potentiate the adverse events of indacaterol. Concomitant hypokalaemic treatment with methylxanthine derivatives, steroids, or non-potassium-sparing diuretics may potentiate the possible hypokalaemic effect of beta2-adrenergic agonists, therefore use with caution. Inhibition of the key contributors of indacaterol clearance, CYP3A4 and P glycoprotein (P gp), raises the systemic exposure of indacaterol up to two fold. The magnitude of exposure increases due to interactions does not raise any safety concerns given the safety experience of treatment with indacaterol in clinical studies of up to one year at doses up to twice the maximum recommended indacaterol dose. **ADVERSE REACTIONS:** The presentation of the safety profile is based on the experience with Ultibro Breezhaler and the individual components. Ultibro Breezhaler showed similar adverse reactions to the individual components. As it contains indacaterol and glycopyrronium, the type and severity of adverse reactions associated with each of these components may be expected in the combination. The most common adverse reactions with Ultibro Breezhaler are: Upper respiratory tract infections, Common: Pyrexia, chest pain, musculoskeletal pain, dyspepsia, dental Caries, gastroenteritis, cough, oropharyngeal pain including throat irritation, dizziness, headache, nasopharyngitis, urinary tract infections, sinusitis, rhinitis, chest Pain, oropharyngeal pain including throat irritation, Uncommon: Fatigue, peripheral oedema, muscle spasm, myalgia, pain extremity, bladder obstruction and urinary retention, dry mouth, pruritis, rash, glaucoma, myalgia, musculoskeletal pain, pruritis/rash, paradoxical bronchospasm, epistaxis, tachycardia, palpitations, hypersensitivity, diabetes mellitus and hyperglycaemia, insomnia. Please refer to SmPC for a full list of adverse events for Ultibro Breezhaler. **LEGAL CATEGORY:** POM **PACK SIZES:** Single pack containing 10x1 or 3x10 hard capsules, together with one inhaler. **MARKETING AUTHORISATION HOLDER:** Novartis Europharm Limited, Frimley Business Park Camberley GU16 7SR, United Kingdom. **MARKETING AUTHORISATION NUMBERS:** EU/1/13/862/003 , EU/1/13/862/007 **Please refer to Summary of Product Characteristics (SmPC) before prescribing.** Full prescribing information is available on request from Novartis Pharma Services Inc, Representative Office Malta P.O Box 4, Marsa, MRS 1000 Malta. Tel: +35621222872 2015-MT-ULT-09-OCT-2015

1. Novartis Europharm Ltd. Ultibro Breezhaler Summary of Product Characteristics.

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DIAGNOSTIC IMAGING OF MASS LESIONS IN THE HAND

PIERRE VASSALLO

Mass lesions in the hand are not common. However, a run of clinical cases that the author encountered in recent weeks prompted him to write on the subject. Lesions of the epidermis and dermis and those of bony origin will not be discussed in this article.

GANGLION CYST

The most common soft tissue mass lesion found in the hand is a ganglion or ganglion cyst as it is sometimes referred to. These lesions originate from tendon sheaths or joint synovial lining following (usually repetitive) trauma. They are clinically hard and well-defined and are usually painful. They tend to move along with movement of the related tendons. Ultrasound is usually sufficient to confirm a ganglion as a fluid-filled well-defined lesion occasionally containing some debris related to a tendon or joint (Fig 1). These lesions frequently resolve spontaneously with rest or they may be ruptured by manual massage. Traditionally, they were smashed with a heavy book. The Bible served this purpose well; in fact ganglion cysts are also known as Bible cysts. Additional treatment options include ultrasound-guided steroid injection and surgical excision.

LIPOMAS

Lipomas were once believed to be rare in the hand, but are now considered common in this location. Most often they are found in subcutaneous layer, but they occasionally occur in deeper layers particularly intramuscularly. Clinically they present as a mass showing insidious growth. Most are solitary and asymptomatic and only come to clinical attention when they are of cosmetic concern or when they become large enough to create mechanical impairment. About 20% of hand lipomas present with pain and tenderness, and less commonly sensory deficit due to nerve impingement. Lipomas appear as well-defined echogenic masses on ultrasound that can be clearly distinguished from surrounding structures (Fig 2). Lipomas show high T1 and low T2 signal that is in contrast to most other solid lesions. Solid tumors are usually further investigated with MRI, which is very useful in identifying tissue type (Fig 3).

SUBCUTANEOUS HAEMANGIOMAS

Subcutaneous haemangiomas consist primarily of a cluster of blood vessels within a solid soft tissue mass. The palm was the most common location in the clinical cases reviewed by the author. Progressive enlargement of the lesion and throbbing pain were the most common symptoms. Characteristic features of haemangiomas include compressibility, poorly defined margins, bluish discolouration of overlying skin, and enlargement of the lesion when the venous return is obstructed or the extremity elevated. Ultrasound shows a soft tissue mass with varying vascularity that may be seen as sparse channels on grey-scale ultrasound (Fig 4a) with possibly a feeding artery on colour Doppler ultrasound (Fig 4b). Haemangiomas are usually surgically excised with ligation of the feeding vessels as distant from the tumor as possible in order to diminish the chances of recurrence.

NERVE SHEATH TUMORS

Nerve sheath tumors may occur at any location in the body where nervous tissue is present. These tumors often affect the function of the nerve, causing pain and disability. A large majority of peripheral nerve tumors are benign and include neurofibromas or schwannomas. Some occur as part of a more generalized condition such as neurofibromatosis or schwannomatosis, both of which are genetic disorders of the nervous system. Malignant nerve sheath tumors are rare; they are more commonly seen in cases of neurofibromatosis type 1. Peripheral nerve sheath tumors are often hypoechoic and may show posterior acoustic enhancement. The presence of peripheral nerve continuity suggests the diagnosis of peripheral nerve sheath tumor (Fig 5). Sonography cannot reliably distinguish neurofibromas from schwannomas.

GIANT CELL TUMORS

Giant cell tumors of the tendon sheath are benign tumors of unknown aetiology arising from the tendon sheath and are considered as a variant of pigmented villonodular synovitis. These lesions usually affect the volar aspect of the first three digits, much less commonly affecting the wrist. On ultrasound, the lesions are usually well-defined and hypoechoic and may be hypervascular on colour Doppler ultrasound (Fig 6). MRI scans show a usually well-defined lesion with low T1 and high T2 signal, demonstrating strong enhancement following intravenous contrast administration (Fig 7). These findings are characteristic of most tendon sheath lesions, and excision biopsy is the only means to obtain a histological diagnosis.

FIBROMAS

Fibromas of the flexor tendon sheath are rare benign tumours, which present as a firm, well-defined mass attached to the tendon sheath. Imaging findings are similar to those of giant cell tumors on both ultrasound and MRI, however fibromas tend to have a lower signal on T2 weighted images and show less enhancement with IV contrast material. On ultrasound they show as flat hypoechoic lesions that follow the tendon sheath and also tend to move with finger movements (Fig 8).

DUPUYTREN'S CONTRACTURE

Dupuytren's contracture is the proliferation of fibrous tissue within the palmar fascia of the hand, which causes subcutaneous nodules on the palmar surface of the distal crease of the hand. This normally progresses to the cords and bands and, finally, leads to the characteristic flexion contracture secondary to fibrous attachments to the underlying tendon sheath. Histologically and on imaging the appearance is similar to flexor sheath fibromas (Fig 9).

FIBROLIPOMATOUS HAMARTOMAS

Fibrolipomatous hamartomas are benign tumors usually affecting infants and less commonly children and young adults. The median nerve is the most commonly affected nerve (80% of cases) but other upper and lower limb nerves may be involved. The most common clinical presentation is that of a soft, slowly enlarging and often asymptomatic mass on the volar wrist frequently present since infancy. Occasionally, nerve compression will lead to symptoms of pain, paresthesia or carpal tunnel syndrome. It is postulated that this is a congenital abnormality of the growth of fibrofatty tissues that causes infiltration and fusiform nerve enlargement. Sonographic findings show hyperechoic tissue (echogenic fatty tissue) surrounding smooth round hypo- or anechoic fascicles. MRI is the preferred imaging modality and shows fusiform nerve enlargement with abundant fibro-fatty tissue surrounding individual nerve fascicles. Enlarged nerve bundles look like serpentine or tubular structures on all imaging modalities (Fig 10). The MRI appearance of fibrolipomatous hamartomas is pathognomonic.

The above article does not claim to cover all differential diagnostic possibilities of soft tissue masses of the hand. However it discusses the more common entities and their imaging features. High resolution ultrasound and MRI are the main imaging modalities that help not only to characterise the lesions, but also to evaluate their relationship to sensitive structures such as arteries and nerves. This information is useful in surgical planning. Some of the lesions have very similar imaging characteristics and biopsy is required in many cases to establish a diagnosis.

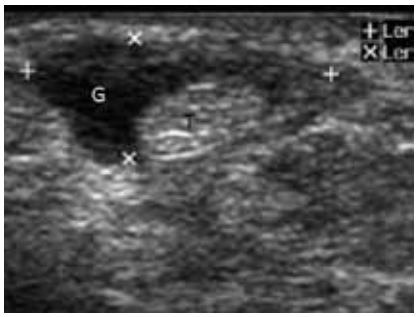


Figure 1. High resolution ultrasound showing a ganglion (G) contiguous with a sheath surrounding the flexor pollicis longus tendon (T)

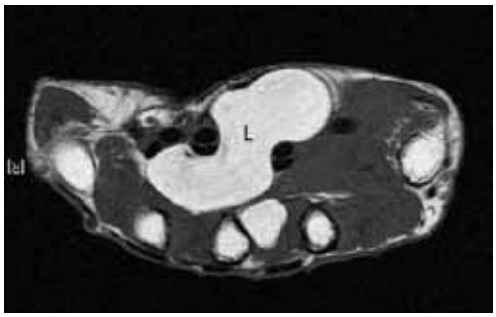


Figure 3. T1 weighted MRI scan through the palm showing a lipoma as a well-defined lesion (L) of high T1 signal that can insinuate itself between normal structure (tendons in this case) and can cross compartments

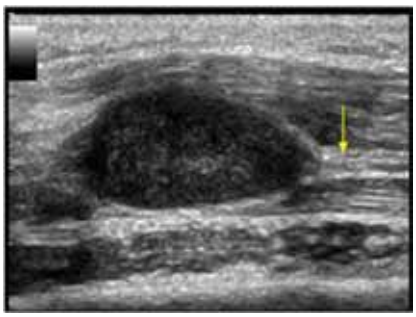


Figure 5. Longitudinal ultrasound scan of a schwannoma of the ulnar nerve. The lesion is well-defined and the continuation of the ulnar nerve can be seen proximal to it (arrow)

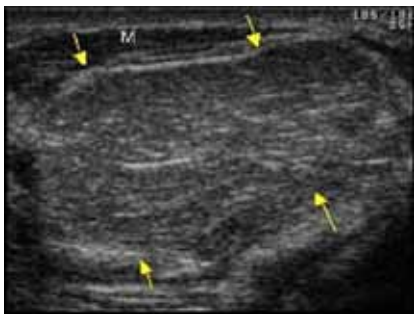


Figure 2. Ultrasound scan of an intramuscular lipoma (arrows) located within the hypothenar muscles (M)

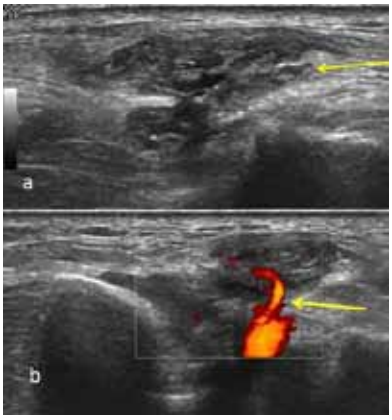


Figure 4. Palmar haemangioma seen on ultrasound as a mostly solid lobulated lesion with sparse vascular channels (a) and with a feeding vessel on colour Doppler scanning (b)

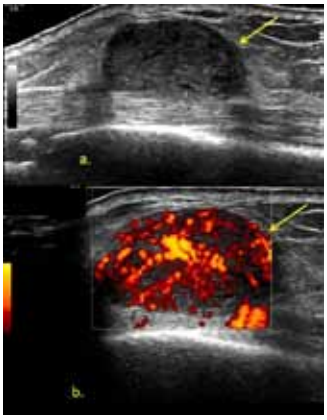


Figure 6. Ultrasound scan shows a giant cell tumor of the flexor pollicis longus tendon. Grey scale image (a) shows a well-defined hypoechoic nodule with increased Doppler flow (b)

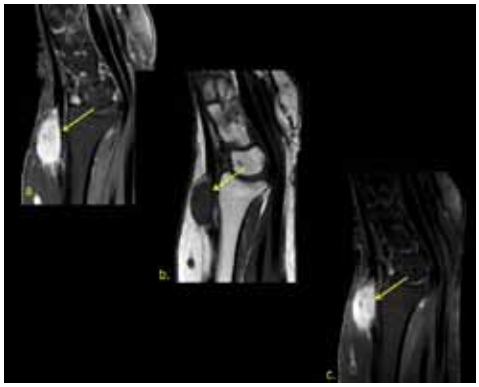


Figure 7. MRI scan of a giant cell tumor related to one of the digital extensor tendons shows a well-defined lesion with low T1 (b) and high T2 (c) signal with strong enhancement following administration of IV contrast material (a)

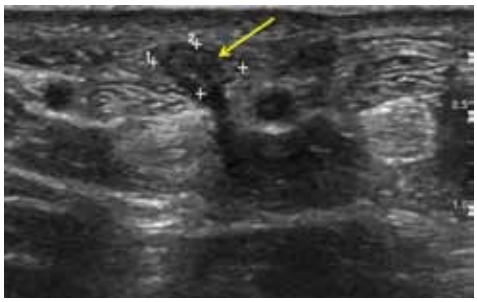


Figure 8. Ultrasound scan of a fibroma of one of the extensor tendon sheaths appearing as a hypoechoic lesion (arrow) that abuts the said tendon sheath and moves with the finger movements

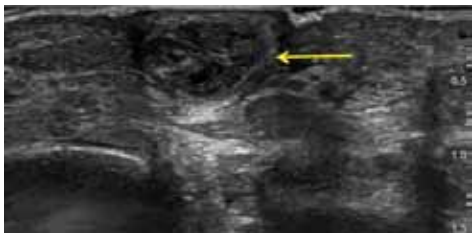


Figure 9. Dupuytren's fibrosis seen on ultrasound as a nodular thickening of the palmar fascia (arrow)

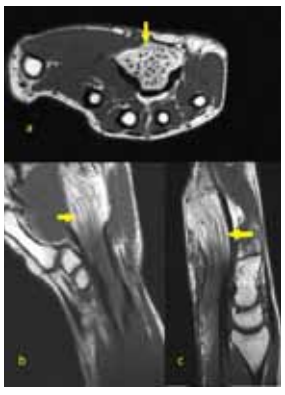
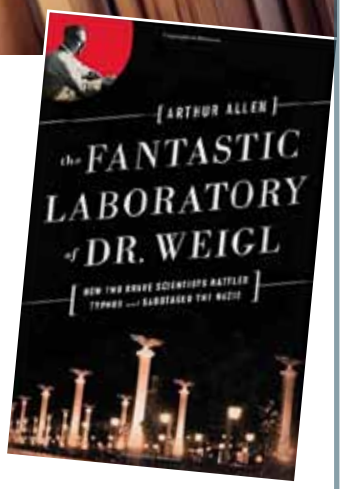


Figure 10. T1 weighted MRI scans in the transverse (a), coronal (b) and sagittal (c) planes showing fusiform enlargement of the median nerve with the individual fascicles of the median nerve separated by abundant high signal fibro-fatty tissue (arrows)

EDITOR'S PICK FOR BOOKWORMS



THE FANTASTIC LABORATORY OF DR WEIGL: HOW TWO BRAVE SCIENTISTS BATTLED TYPHUS AND SABOTAGED THE NAZIS

Arthur Allen
W. W. Norton & Company Inc.; 384 pages; $16.38
Published in April 2015

Few diseases are more gruesome than typhus. Transmitted by body lice, it afflicts the dispossessed – refugees, soldiers, and ghettoized peoples – causing hallucinations, intense headaches, boiling fever, and often death. The disease plagued the German army on the Eastern Front and left the Reich desperate for a vaccine. For this they turned to the brilliant and eccentric Polish zoologist Rudolf Weigl.

In the 1920s, Weigl created the first typhus vaccine using a method as bold as it was dangerous for use in humans. The astonishing success of Weigl's techniques attracted the attention and admiration of the world - giving him cover during the Nazi's violent occupation of Lviv. His lab soon flourished as a hotbed of resistance. Weigl hired otherwise doomed mathematicians, writers, doctors, and other thinkers, protecting them from atrocity. The team engaged in a sabotage campaign by sending illegal doses of the vaccine into the Polish ghettos while shipping gallons of the weakened serum to the Wehrmacht.

Among the scientists saved by Weigl, who was a Christian, was a gifted Jewish immunologist named Ludwik Fleck. Condemned to Buchenwald and pressured to re-create the typhus vaccine under the direction of a sadistic Nazi doctor, Erwin Ding-Schuler, Fleck had to make an awful choice between his scientific ideals or the truth of his conscience.

Drawing on extensive research and interviews with survivors, Allen tells the harrowing story of two brave scientists – a Christian and a Jew – who put their expertise to the best possible use, at the highest personal danger.

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Prepared: October 2015
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