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THESYNAPSE

THE MEDICAL PROFESSIONALS' NETWORK

- Malta Chamber of Pharmacists AGM
- Spinal Fractures in Malta
- Comparison of hypertension in Tanzania and Malta
- Meeting Franklin Camilleri

Volume 14 Issue 01 ISSN number 2313-8084

For your high CV -risk adult patients with mixed dyslipidaemia to reduce TG and increase HDL-C levels when LDL-C levels are adequately controlled with the corresponding dose of simvastatin

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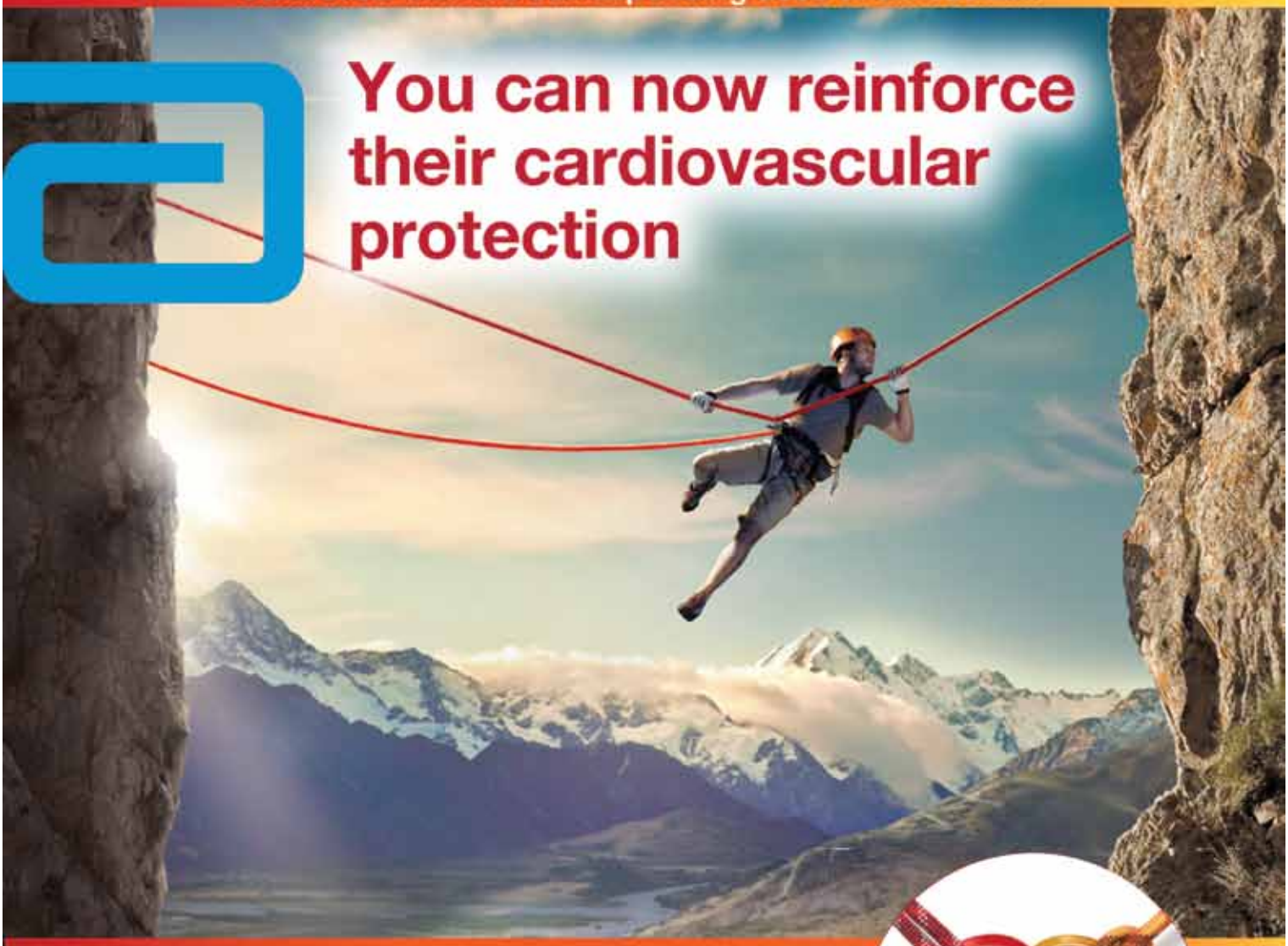

NEW

Fixed-dose combination therapy

CHOLIB 145 mg/20 mg and 145 mg/40 mg FILM-COATED TABLETS: PRESCRIBING INFORMATION

Refer to the Summary of Product Characteristics for full information
Presentation: Cholib 145 mg/20 mg film-coated tablets containing 145 mg of fenofibrate and 20 mg of simvastatin. Cholib 145 mg/40 mg film-coated tablets containing 145 mg of fenofibrate and 40 mg of simvastatin.**Indications:** Cholib is indicated as adjunctive therapy to diet and exercise in high cardiovascular risk adult patients with mixed dyslipidaemia to reduce triglycerides and increase HDL-C levels when LDL-C levels are adequately controlled with the corresponding dose of **simvastatin** monotherapy. **Dosage and Administration:** Secondary causes of hyperlipidaemia should be adequately treated before Cholib is considered and patients should be placed on a cholesterol and triglycerides-lowering diet which should be continued during treatment. The recommended dose is one tablet per day and should be taken whole with water. **Contraindications,** Warnings, Precautions etc: Contraindications: Hypersensitivity to the active substance, excipients, peanuts or soya, known **photoallergy** or phototoxic reaction with fibrates or ketoprofen, active liver disease or unexplained persistent elevations of serum transaminases, known gall bladder disease, chronic or acute pancreatitis with the exception of acute pancreatitis due to severe hypertriglyceriaemia, moderate to severe renal insufficiency, concomitant administration of fibrates, statins, danazol, ciclosporin, potent cytochrome P450 (CYP) 3A4 inhibitors, fusidic acid, grapefruit juice, paediatric population (below 18 years), pregnancy or **breastfeeding,** history of myopathy and/or rhabdomyolysis with statins and/or fibrates or confirmed creatine phosphokinase elevation under previous statin treatment. Amiodarone, verapamil, amlodipine or diltiazem is contraindicated with Cholib 145 mg/40 mg only. *Warnings and precautions:* Muscle – skeletal muscle toxicity, including rare cases of rhabdomyolysis with or without renal failure has been reported and reduced function of OATP transport proteins can increase this risk. Patients should be advised of the **risk** and told to report any unexplained muscle pain, tenderness or weakness. Caution should be exercised in patients with pre-disposing factors: elderly (> 65 years, females, renal impairment, uncontrolled hypothyroidism, hypoalbuminaemia, personal or familial history of hereditary muscular disorders, previous toxicity with a statin or a fibrate, alcohol abuse. If myopathy is suspected for any other reason, treatment should be discontinued. Therapy should be temporarily stopped prior to major surgery. Hepatic disorders - Transaminase levels should be monitored and therapy discontinued if necessary, therapy should be discontinued if hepatitis is confirmed, and used with caution in patients who consume substantial quantities of alcohol. Pancreatitis – may represent a failure of efficacy in patients with severe hypertriglyceridaemia, induced pancreatic enzyme increase or obstruction of the bile duct. Renal – use with caution in patients **with mild renal insu**fficiency, treatment should be interrupted when creatine level is 50% above the upper limit of normal. Interstitial lung disease – cases have been reported with some statins and fenofibrate, therapy should be discontinued if suspected. Diabetes mellitus - statins may increase blood glucose and at-risk patients should be monitored. Veno-thromboembolic events – caution in patients with history of pulmonary embolism. Excipients – Cholib contains lactose and sucrose, patients with **rare** hereditary problems of galactose and/or fructose intolerance, Lapp lactase deficiency, glucose-galactose malabsorption or sucrose-isomaltase insufficiency should not take this medicine. Patients allergic to sunset yellow FCF (E110) should not take this medicine (applicable to Cholib 145 mg/20 mg). *Drug interactions:* Cholib is contraindicated with the following – itraconazole, ketoconazole, fluconazole, posaconazole , erythromycin , clarithromycin , telithromycin , HIV protease inhibitors (e.g. nelfinavir), **nefazodone,** danazol, ciclosporin, gemfibrozil, other statins and other fibrates. Patients should avoid grapefruit juice and should be closely monitored if taking niacin, colchicine, Vitamin K antagonists (INR monitoring) or glitizones. Taking rifampicin may decrease the efficacy of Cholib. Patients taking amiodarone, verapamil, diltiazem, amlodipine should not exceed 145 mg/20 mg per day. **Fertility, Pregnancy and Lactation:** Should not be used during pregnancy or breastfeeding. No **fertility** data available. **Ability to Drive and Operate Machinery:** Dizziness has been reported as a rare side-effect. **Side Effects:** *Side effects observed with co-administration of fenofibrate and simvastatin:* Very common - blood creatinine increased. Common - upper respiratory tract infection, gastroenteritis, platelet count increased, alanine-aminotransferase increased. Uncommon - dermatitis and eczema. *Side effects observed with the use of fenofibrate:* Very common – blood **homocysteine** level increased. Common – gastrointestinal signs and symptoms (abdominal pain, nausea, vomiting, diarrhoea, flatulence) and ransaminases increased. Uncommon – headache, thromboembolism (pulmonary embolism, deep vein thrombosis), pancreatitis, cholelithiasis, cutaneous hypersensitivity (e.g. rash, pruritus, urticaria), muscle disorders (e.g. myalgia, myositis, muscular spasms and weakness) and sexual dysfunction. Rare – haemoglobin decreased, white blood cell count decreased, hypersensitivity, alopecia, photosensitivity reactions, rhabdomyolysis with or without renal failure and blood urea increased. Frequency not known – complications of cholelithiasis (e.g. cholecystitis, cholangitis, biliary colic etc) and severe cutaneous reactions (e.g erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis etc.). *Side effects observed with the use of simvastatin:* Rare – anaemia, paresthesia, dizziness, peripheral neuropathy, memory impairment/memory loss, constipation, dyspepsia, gamma- glutamyltransferase increase, hypersensitivity syndrome, myopathy, asthenia, blood alkaline phosphatase increased and blood creatine phosphokinase level increase. Very rare – insomnia, hepatitis/jaundice and hepatic failure. Frequency not known – Diabetes Mellitus, sleep disorder including nightmares, depression, interstitial lung disease, tendinopathy, erectile dysfunction, glycosylated haemoglobin increased and blood glucose increased.

Marketing Authorisation Holder: Abbott Healthcare Products Limited

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Legal Category: POM

Further information is available from: BGP Products Ltd, Abbott House, Vanwall Business Park, Vanwall Road, Maidenhead, SL6 4XE, UK. Tel: 01628 773355.

Date of Last Review: 15th January 2015

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TEIXOBACTIN
THE TREATMENT OF AN ACHILLES HEEL?

The first time I heard about Maine was by watching *Murder, She Wrote*. This was an American television series, starring Angela Lansbury [as you read, this 89 year old woman is still actively interpreting Madame Arcati on stage in *Blithe Spirit*] as detective Jessica Fletcher. Fletcher was a resident of Cabot Cove, a coastal town in Maine; the fictitional 'Cabot Cove' name was derived from the name of an actual inlet in Kennebunkport, Maine. However, this year I encountered Maine in a very different context ... *Nature.* A most interesting article, accessible on *www.nature.com* hails Maine as the cradle of a new antibiotic, teixobactin.

As you know, modern antibiotics have been heralded by the marketing of penicillin in the 1940s. Although Sir Alexander Fleming, who discovered penicillin, warned of the dangers of resistance way back in his Nobel prize speech in 1945, few would have thought of such resistance to be the achilles heel of antibiotics back then. Nonetheless, it has resulted in a shortfall of medical armamentarium when dealing with infections. We are partly to blame for this, considering the overuse of antibiotics, illegal over-the-counter selling of antibiotics as well as agricultural misuse. Actually, last December the UK has published

Antimicrobial Resistance: Tackling a crisis for the health and wealth of nations, where it is being predicted that by 2050, antibiotic resistance would cost the world up to €88,000,000,000,000 and a reduction of 2% to 3.5% in global GDP - *www.jpiamr.eu.* This initiative has been heralded by the UK's Prime Minister, David Cameron.

Returing to teixobactin, researchers at the National Institutes of Health and the German government have developed a new technology, the iChip, which is a lattice of tiny wells. Researchers dip the chip in a bacterial sample [diluted soil] mixed with agar to trap cells in each well, after which it is covered with a permeable membrane to lock the sample inside. The iChip is then placed in the bacteria's original environmental habitat [soil]. Using this technique, the researchers were able to screen 10,000 bacteria, previously unculturable. This is how they discovered a new bacteria, *Eleftheria terrae which is* the source of teixobactin, an 11-residue, macrocyclic depsipeptide. This was found to be a novel inhibitor of cell wall synthesis by binding to a highly conserved motif of lipid II (precursor of peptidoglycan) and lipid III (precursor of cell wall teichoic acid), leading to lysis of vulnerable bacteria. It seems to work on Gram-positive bacteria only, including MRSA and mycobacterium tuberculosis.

Teixobactin's next step is clinical trials in order to investigate the safety and efficacy of the medicine. Although the process may take up to 15 years, in this case, I assume that modelling and simulation will be used to extrapolate and interpolate safe and effective drug doses in diverse clinical conditions. This will shorten the authorisation process.

However, the million dollar question is the following ... if teixobactin ever manages to reach the market, will it be prostituted like all the other antibiotics which have previously been heralded as game-changers?

Ian Ellul

Cover: The Royal Navy Hospital in Mtarfa was a British naval hospital. It was the main hospital for British Forces in the eastern Mediterranean until the British left Malta in 1979.

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THESYNAPSE 18 ANNIVERSARY

To coincide with the 18th anniversary of the launch of TheSynapse, and to complement its already very wide range of services offered to users, TheSynapse has recently reached another milestone by launching TheSynapse Video Section, bringing you local experts directly to your desktop or mobile device.

Available on demand and offering a vast range of topics for the busy medical professional, TheSynapse Video Section will offer regular medical education updates, as well as updates on recent medical developments that are most significant to the rapid evolution of the medical field.

We are very grateful to the speakers, all respected and eminent experts in their respective fields, who accepted to participate in these programmes. We are sure that this series will rapidly grow to be a significant source of e-learning and continuing medical education to medical professionals in Malta and abroad.

TheSynapse video section is available on thesynapse.net/videos

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ISSUE GUIDE

TheSynapse

ALEXANDER BORG

RECENT ADVANCES IN CARDIOVASCULAR IMAGING PART II

In this second instalment I will focus on the use of tomographic imaging, namely cardiac computed tomography (CCT) and cardiovascular magnetic resonance imaging (CMR), in the structural and functional assessment of the cardiovascular system. Although Computed Tomography and Magnetic resonance have been in clinical use over the last 40 years, it is only through more recent advances in technology that imaging of a constantly moving structure like the heart has become possible with sufficient acquisition speed and spatial resolution. Now that this technology has become an important component of mainstream cardiology, it is imperative that all medical professionals understand the role and capabilities of CCT and CMR in order for patients to benefit from the exquisite diagnostic potential of this non-invasive technology.

CARDIAC COMPUTED TOMOGRAPHY

The turning point which led to cardiac imaging is the development of helical CT in 1997. Further improvements in gantry rotation speed, image processing techniques and detector size have enabled rapid acquisition of images of coronary arteries with sufficiently high spatial resolution (sub-millimetre) and low motion artefact to be able to resolve presence of atherosclerotic plaque and luminal stenosis. CCT differs from imaging of other organs in that acquisition is gated

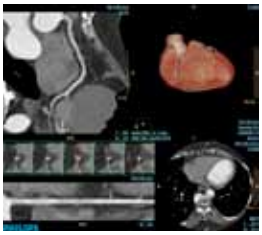

Figure 1: Output from CCT coronary analysis software showing a curved reconstruction of a normal right coronary artery (top left), a volume-rendered 3D reconstruction of the coronary vessels and heart (top right) and stenosis assessment (bottom left).

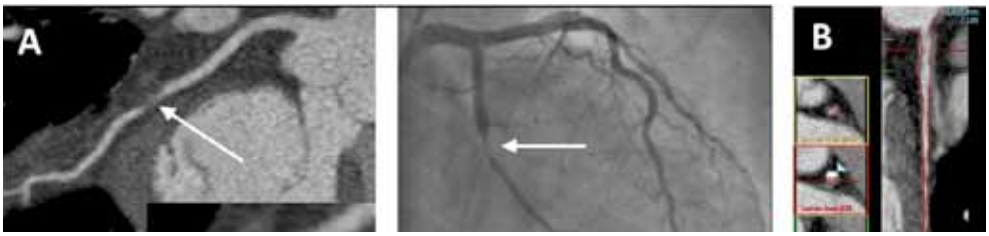

Figure 2: A: CT coronary angiogram showing non-calcified plaque causing severe narrowing of the left circumflex artery (left), with corresponding appearance on an invasive coronary angiogram (right); B: A calcified lesion (bright, high attenuation appearance – blue arrowhead) causing mild luminal obstruction in the left anterior descending artery, shown on quantitative coronary analysis software.

ONE OBVIOUS ADVANTAGE OF CCT ARE ITS NON-INVASIVE NATURE, AVOIDANCE OF POTENTIALLY LIFE-THREATENING COMPLICATIONS, AND DRASTICALLY REDUCED IN-PATIENT STAY

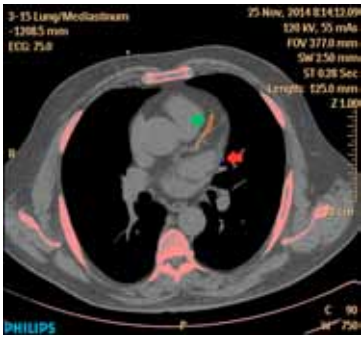

Figure 3: A coronary calcium CT scan, showing automatically highlighted area of calcified plaque in the left anterior descending (green arrow) and left circumflex coronary arteries (red arrow).

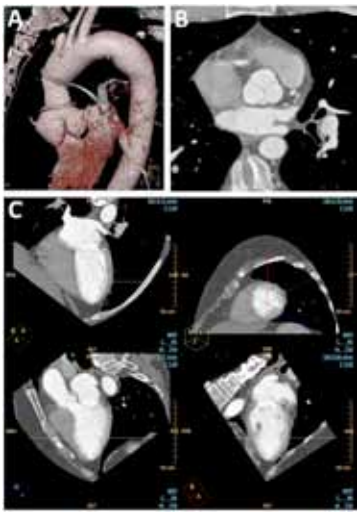

Figure 4: Non-coronary applications of cardiac CT. A: Volume-rendered 3D reconstruction of aorta; B: Axial view of aortic valve leaflets; C: Multi-planar imaging of the left ventricle.

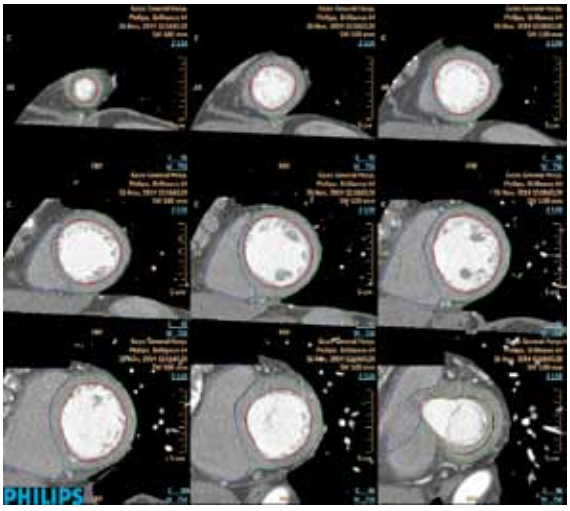

Figure 5: Structural and functional assessment of the ventricles on CT scan. Several axial views of the ventricles are obtained from base to apex of the heart. Endocardial borders are automatically drawn by edge-detection algorithms. The areas of the delineated chambers in each view are combined to generate volumes, mass and ejection fraction.

to the patient's ECG in order to acquire images during phases when cardiac motion is minimal, and in order to reconstruct images according to the phase of the cardiac cycle. The patient is also instructed to breath-hold for a few seconds to minimise respiratory motion.

The spatial resolution of modern CCT rivals that obtained in conventional invasive coronary angiography. However, the main advantage of CCT is the ability to visualise and characterise atherosclerotic plaque, even when it does not cause significant luminal obstruction. Invasive angiography acquired during the intracoronary injection of radio-opaque contrast media, on the other hand, only reveals the luminal calibre, and fails to visualise non-calcified plaque which does not impinge on the lumen. Yet the presence of such plaque is known to be a precursor of acute coronary syndromes. The other obvious advantages of CCT are its non-invasive nature, avoidance of potentially life-threatening complications, and drastically reduced in-patient stay (the whole procedure rarely takes more than 20 minutes).

The main use of CCT is in the detection of coronary artery disease (CAD) in patients with chest pain deemed to be at low to intermediate risk of having significant CAD (figures 1 and 2). The rationale behind this is two-fold: one would like to benefit from the CCT's high negative predictive value for CAD in this subgroup and, secondly, the careful selection of patients who are unlikely to need further downstream exposure to radiation due to invasive angiography and percutaneous revascularisation. CCT coronary angiography is also useful in the presence of equivocal results from stress ECG or functional imaging (stress echocardiography or nuclear perfusion scans) in patients with suspected angina.

CCT has two other important roles. The first is the quantification of coronary calcium for the purpose of cardiovascular risk stratification in asymptomatic patients with intermediate cardiovascular risk (based on presence of cardiovascular risk factors and use of risk scores such as Framingham risk score or Heart Score) or in patients with a positive family history of premature ischaemic heart disease. The presence of coronary calcification is practically synonymous with the presence of atherosclerotic plaque, and can be quantified by scores based on the degree of attenuation and area of the lesion (Agatston score) (figure 3) An age- and gender-based percentile can be derived for the patient based

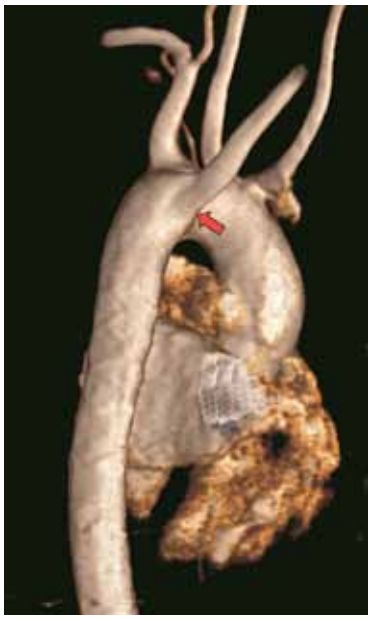

Figure 6: Volume-rendered reconstruction of a contrast-enhanced aortogram obtained by CMR. The image represents a dorsal view of the aortic arch, showing the origin of an aberrant retro-oesophageal right subclavian artery from the posterior aspect of the distal aortic arch (red arrow) in a patient with Turner's syndrome.

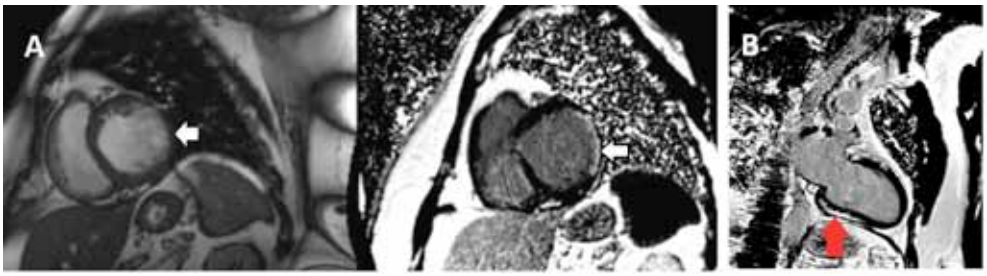

Figure 7: Late enhancement images in the diagnosis of heart failure. A: Patient with a thinned lateral wall of the left ventricle. Images obtained a few minutes after gadolinium contrast injection (late enhancement images) reveal a high signal extending from the subendocardium and involving up to 50% of the myocardial thickness, diagnostic of a myocardial infarction (white arrows); B: Late enhancement image of another patient with heart failure, showing mid-myocardial late enhancement in the inferior wall (red arrow) diagnostic of a non-ischaemic cardiomyopathy, probably a consequence of previous myocarditis.

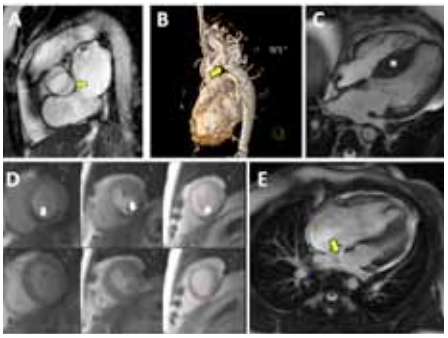

Figure 8: The many uses of CMR. A: Bicuspid aortic valve (yellow arrow). B: Severe narrowing of the distal aortic arch in a patient with coarctation of the aorta (yellow arrow). Also note prominent collateral vessels. C: Localised thickening of the interventricular septum in a patient with hypertrophic cardiomyopathy (asterisk). D: Perfusion imaging of the left ventricle in a patient with suspected angina, acquired during first-pass gadolinium infusion. The lower three short axis images were obtained at rest, and show homogenous contrast uptake. However, there is relatively low signal in the inferior and inferoseptal segments (white arrows) in the upper 3 short axis images, obtained during adenosine stress. This is diagnostic of ischaemia in the right coronary artery territory. E: A secundum atrial septal defect (yellow arrow) seen in a four-chamber view.

on nomograms derived from population studies. The resulting refined risk stratification may aid decisions on starting primary prevention medication, based on the amount of calcification. A CT calcium score may tip the risk-benefit ratio one way or the other if you are not sure whether your asymptomatic patient may derive a net benefit from statins or aspirin for primary prevention. In addition, a CT calcium score may prove useful as a gatekeeper in patients with non-acute chest pain with low probability of CAD – while the absence of calcium implies an excellent prognosis in this subgroup of patients and obviate the need for further imaging, the presence of any degree of calcium may prompt the imager to proceed with CT angiography.

The second major role of CT is in the assessment of heart chambers, valves, pericardium, congenital heart disease and major blood vessels (figure 4). Such scans are usually indicated when information cannot be obtained from non-radiation techniques like echocardiography or CMR (commonly due to poor echocardiographic windows and/or presence of metal implants – like cardiac pacemakers – which preclude a CMR). Although this involves considerably more radiation, X-rays can be emitted throughout the cardiac cycle to obtain systolic and diastolic images, allowing calculation of ejection fraction and stroke volume (figure 5)

Like invasive angiography, CCT entails exposure to ionising radiation. However, careful patient selection, pre-procedural beta-blockers to reduce the patient's heart rate, use of special acquisition techniques, and other technological improvements have dramatically reduced the radiation dose. With a state-of-the-art scanner in a well selected patient, one should expect an effective dose of 3 mSv, which compares favourably with invasive diagnostic coronary angiography (2-7 mSv) and nuclear perfusion imaging (6-15 mSv).

CARDIOVASCULAR MAGNETIC RESONANCE IMAGING

Like CCT, CMR is based on well-established technology which had to await further technological innovations before becoming feasible for cardiac imaging. CMR is a non-invasive technique which does not utilise ionising radiation. Magnetic resonance imaging is based on the behaviour of hydrogen nuclei, mostly within water molecules, when placed in a magnetic field generated by a superconductor magnet. Excitation by radiofrequency signals temporarily deflects magnetisation of these hydrogen nuclei. While this altered magnetisation returns to its equilibrium state, a current is induced in a receiver coil, generating the magnetic resonance signal which is used to construct an image.

The beauty of CMR is that excellent intrinsic contrast, without administration of exogenous contrast, is generated between tissues that have different chemical composition. However, exogenous contrast like gadolinium is also administered to produce high quality angiograms (figure 6) and to determine the cause of heart muscle disease (figure 7). By being able to provide functional information (blood flow velocity and stroke volume), CMR is a truly "one-stop shop" for addressing all cardiac problems. The other advantage of CMR over echocardiography is the independence of image quality from body habitus and unusual anatomy; indeed imaging planes can be prescribed in any direction and are not limited by the factors that impede ultrasound transmission through body tissues.

CMR provides a wealth of structural and functional information, ranging from myocardial abnormalities, valve disease, aortic pathology, cardiac tumours and congenital heart defects (figures 8 and 9). Perfusion CMR is a technique for detecting cardiac ischaemia; imaging is carried out during gadolinium infusion at baseline and during vasodilator stress with adenosine. Hypoperfused myocardium manifests as low signal areas during stress imaging, which are not visible on the resting images (figure 8D). A common indication is to assess the cause of heart failure, and to assess the viability of heart muscle - in patients with myocardial infarction - to guide revascularisation of CAD (figure 7). The severity of valvular stenosis and regurgitation can be confirmed with CMR (avoiding the need for invasive pressure measurements) by measuring transvalvular velocities and regurgitant volumes. Another important role of CMR is in the non-invasive detection of cardiac iron overload in patients who require lifelong blood transfusions, as in thalassaemia major, prompting timely administration of life-saving chelation therapy. Finally, since CMR does not involve radiation, it is ideal for lifelong follow-up of patients with inherited cardiovascular conditions and operated congenital heart disease patients, most commonly patients with repaired tetralogy of Fallot and patients with Marfan's syndrome and dilated aortas.

CMR does have some important limitations. Patients with certain metallic implants cannot enter the scanner due to the deleterious effect of the strong magnetic field. Cardiac pacemakers are a particularly common problem, though most companies now produce MRI-conditional pacemakers which can be placed in a scanner provided certain precautions are taken. Another problem is the duration of the scan - patients are expected to lie still for about 45 minutes on average. Difficulties in suspending respiration and arrhythmias can affect image quality. Claustrophobia is a real problem, though sedation and use of wide-bore scanner systems have proved to be helpful. Large patients may not fit in the scanner. Of note, patients who cannot have an MRI because of these reasons can be considered for CT scanning, as discussed above. Finally, gadolinium contrast is contra-indicated in patients with severe renal dysfunction although, fortunately, there are non-contrast alternatives available in most situations.

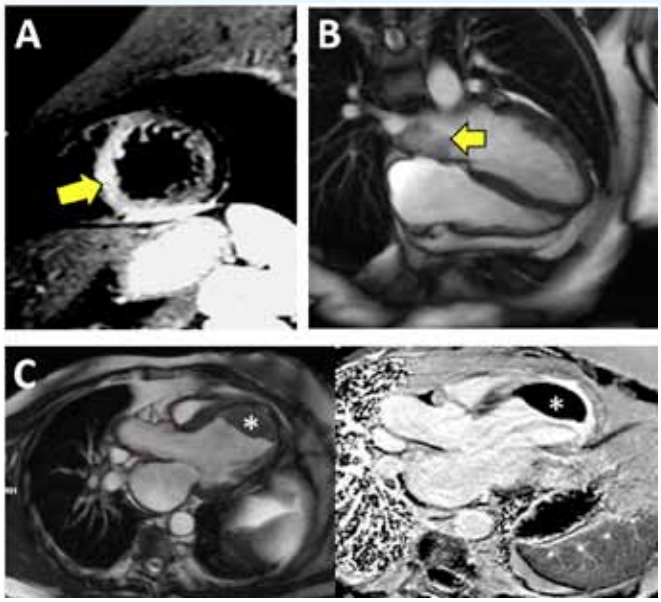

Figure 9: Other uses of CMR. A: Oedema pulse sequence showing high signal in the interventricular septum (yellow arrow) diagnostic of myocardial inflammation in a patient with active myocarditis. B: An atrial myxoma (yellow arrow) attached to the interatrial septum on the left atrial side. C: An intracavitary mass at the apex of the left ventricle (asterix). The total absence of contrast uptake after contrast injection (right image), resulting in very low signal, confirms the presence of a large thrombus.

Cardiac imaging has changed modern cardiology practice, and continues to do so as technology improves. The limitations of echocardiography and the need for invasive imaging have been eliminated for a large subgroup of our patient population. The techniques described are well-grounded in science and practical experience. In these two articles I have addressed the role and indications of these new cardiac imaging technologies, most of which are already available in Malta.

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MALTA CHAMBER OF PHARMACISTS AGM

MARY ANN SANT FOURNIER

The Malta Chamber of Pharmacists held its annual general meeting on Friday 19 December 2014.

During the meeting, elections were held for a new Executive Council. Mary Ann Sant Fournier was re-elected president, whilst the council members Max Borg Millo, Claire Calleja (Shaw), Mary Anne Ciappara, Joseph Grima, Margaret Parascandolo and John Vella were also re-elected. Vice-president Antoine Sciberras stepped down and did not stand for re-election whilst Anthony Sammut was not re-elected. Whilst thanking Mr Sammut and Mr Sciberras for their sterling contribution to the Council and Chamber for a number of years, the Council welcomes Marisabelle Bonnici and Claire Shoemake as newly elected council members.

During the meeting, the Secretary of the Chamber, Max Borg Millo presented the administrative report which dwelt on the intensive work of the Council in 2013 and 2014, including the establishment of a working rapport with the new Administration. The Council worked intensively to negotiate and oversee the inception of a professional indemnity insurance cover specifically for pharmacists. The Working Committee on the development of Community Pharmacy produced and issued Guidelines on Emergency Prescribing as well as a Joint Circular to doctors and pharmacists on Prescribing and Dispensing legislation. The Working Comittee also made proposals for the amendments of the Medicines Act and subsidiary legislation with a view to introduce prescribing rights for pharmacists together with a proposed pharmacist medicines list. These have been forwarded by the Council to the Authorities for discussion and implementation. The Council annnounced upcoming meetings for members with the participation of the Government's Consultant, Mr Mike Farrugia, on the opening of preliminary discussions on a Service level Agreement emanating from the POYC MOU signed in 2007, together with the Government's electoral promise of the inception of a Domiciliary delivery of POYC medicines to over-70's who are homebound.

In her presidential Address, Mary Ann Sant Fournier presented and thanked the outgoing council which consists of committed pharmacists who have volunteered to work at great personal sacrifice for the good of the pharmacy profession and its members.

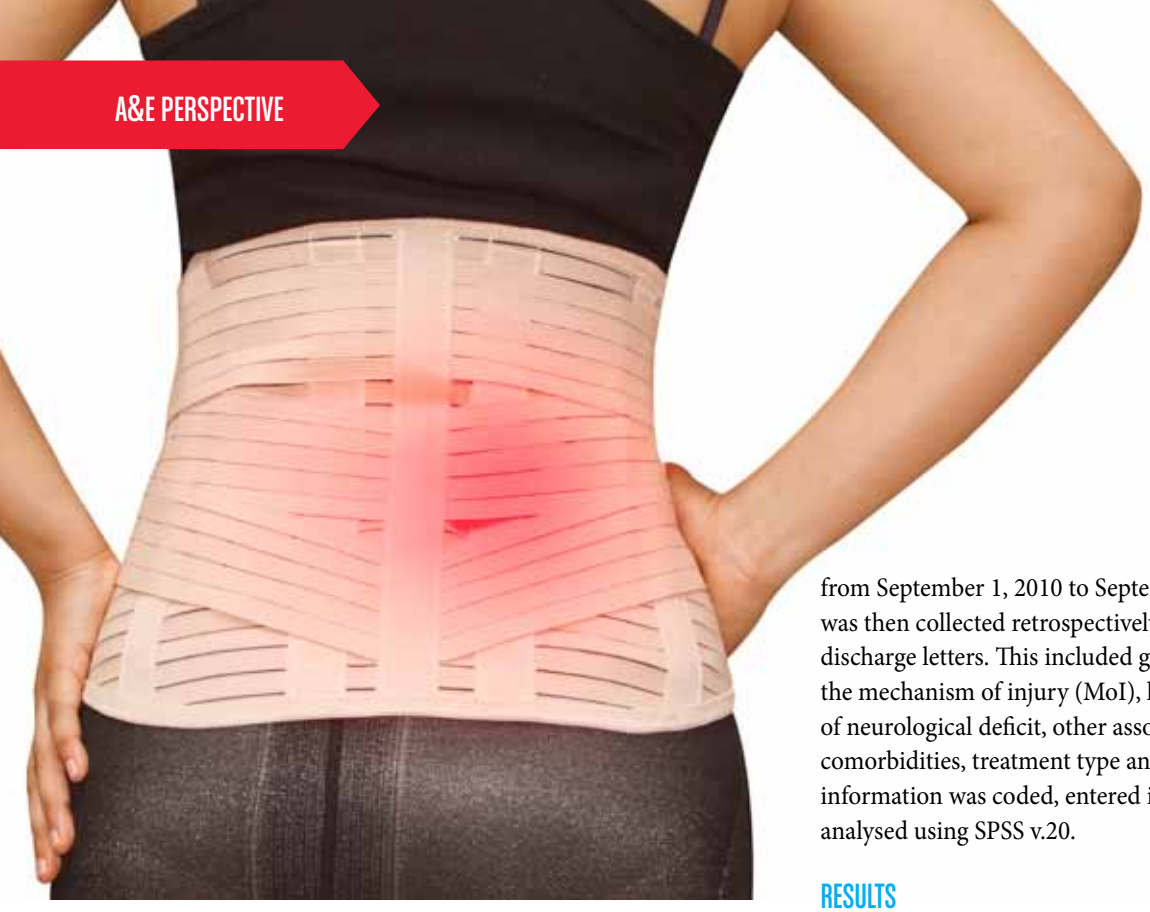
She emphasised the importance of a unified profession and that the incoming council should uphold the independence of the Kamra. She dwelt on highlights of the landmark achievements of the Chamber through its Councils, including:

- the attainment of the professional status of pharmacists in Government service, with the first-in-history defined career progression structure; and the negotiations within the framework of the transposition of the EU Acquis Legislation which culminated in the enactment of the Medicines Act, which included:
  - the inception of the principle of geo-demographic organisation for the opening of pharmacies,
  - a clearly defined role of the community pharmacist,
  - the introduction of the new exclusive role of the pharmacist as a responsible person in the wholesale distribution of medicinal products,
- the Health Care Professions Act, with the new composition of the Pharmacy Council with more elected and appointed Pharmacist representation, and
- the innovative patient focused agreement on the decentralisation of the dispensing of NHS medicines to the pharmacy/pharmacist of the patients' choice (POYC) together with the agreement on the Pharmacy Licensing Regulations.

She said that the incoming Council would find that the Chamber has made an important thrust for the achievement of Pharmacist's Prescribing Rights and other matters related to Prescriptions & Dispensing.

The President called on members present to make the right choice for the Chamber's and the profession's future, which is now.

GLENN ABELA
PAUL CALLEJA



SPINAL FRACTURES IN MALTA OVER ONE YEAR

INTRODUCTION

Spinal fractures, particularly those associated with spinal cord injuries, give rise to significant morbidity and mortality.[1] Early recognition and adequate management are paramount to minimalize the two. This descriptive study reviews the cases diagnosed with a vertebral fracture at the Accident and Emergency Department over a one year period including the patients' demographic characteristics and looks into the management instituted. It also highlights the factors which may be associated with a prolonged hospital stay.

METHODOLOGY

Permission to carry out this study was sought from and granted by the Data Protection Officer at Mater Dei Hospital and the consultant caring for these patients. Cases of vertebral fractures were identified by reviewing the reports of spinal imaging requested at the Accident and Emergency Department from September 1, 2010 to September 1, 2011. Information was then collected retrospectively from the patients' files and discharge letters. This included general demographic data, the mechanism of injury (MoI), level of fracture/s, presence of neurological deficit, other associated injuries or patients' comorbidities, treatment type and length of hospital stay. The information was coded, entered into a MS Excel spreadsheet and analysed using SPSS v.20.

RESULTS

There were 71 cases of spinal fractures over the one year period. Forty-two (59.15%) were males and 29 (40.85%) were females, with the most prevalent age group being 21-30 years (18 patients, 25.35%), followed by the 61-70 age group (15 patients, 21.27%). Mean age was 47.46 years. The highest number of vertebral fracture admissions took place in February and August, when there were 10 cases in each of these months. December had the lowest number of such admissions: only 2 patients.

Seventy patients had a traumatic MoI, while only one had a fracture which was pathologic in origin. The commonest trauma causing a vertebral fracture was a fall from height of more than 2 metres (20 cases, 29.58%). A fall from height less than 2 metres was the MoI in 9 patients (12.68%) while a fall from own height, sea-related injuries and a motor vehicle accident accounted for 10 cases (14.08%) each. Another 11 patients had miscellaneous MoIs. The pathologic fracture case was diagnosed as multiple myeloma on subsequent investigations.

Neurological deficit was present in only 7 cases (9.86%). Nineteen patients (26.76%) had other injuries associated with the fracture and 38 patients (53.52%) had one or more comorbidities. The commonest comorbidities were cardiovascular (29.03%).

Fifty-seven cases (80.28%) were managed conservatively: 22 (30.99%) without a brace, 33 (46.48%) with a brace and two (2.82%) with traction and a brace. Thirteen patients (18.31%) were treated operatively and in most (12 patients) this was carried out using a posterior approach. Mean length of hospital stay was of 8.9 days, with a range of 1 to 89 days. The commonest length of stay (the mode) was of 3 days and 52.1% were hospitalized for 5 days of less.

Fifteen patients (21.13%) had fractures at more than one level, totalling 95 fractures in all subjects. Of these, most fractures

were thoracolumbar (levels Th10 to L2) with 60 fractures (68.84%), followed by lumbar (L3 to L5) with 17 fractures (17.89%) and cervical (C1 to C7) with 16 fractures (16.84%). There were only 2 (2.11%) thoracic fractures (T1 to T9).

The AO (Arbeitsgemeinschaft für Osteosynthesefragen) system of vertebral fractures was used to classify the injuries. However, this system classifies fractures of the vertebral body fractures of the thoracolumbar region only, so 24 fractures were excluded (25.26%): 4 pathologic in origin (in the multiple myeloma patient), 4 which involved parts of the vertebrae other than the body, and the cervical fractures. Of the remaining 70 fractures, 66 involved the vertebral body only: 47 A1 (wedge) fractures (49.47%), 7 A2 (split) (7.37%) and 12 A3 (burst) (12.63%). The other 5 injuries (5.26%) extended to both the vertebral body and adjacent bone structures.

The data was analysed using SPSS v.20 using a 95% confidence interval to correlate various factors with the length of hospital stay. Mean length of hospital stay was higher for males (9 days), the 51 to 60 age group (13 days), patients whose MoI was a motor vehicle accident (12 days), those who had a neurological deficit (15 days) and patients who were treated operatively (12 days). However, none achieved statistical significance.

DISCUSSION

In the cohort investigated above, vertebral fractures were commoner in males and in people at both ends of age distribution. The mean age of 47.46 years was similar to that in a European cohort (45.5 years) but in the latter a larger proportion of men were affected (64.9%).[1] This was also true in China where the male-to-female ratio was of 2.33:1.[2]

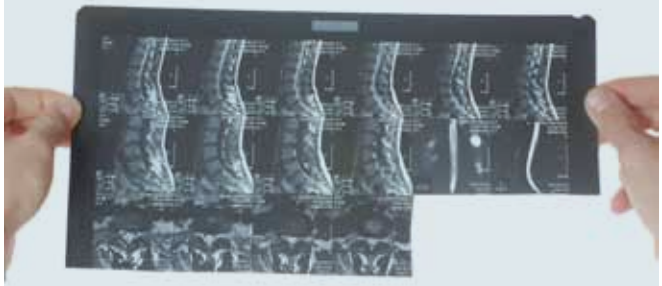
The study identifies trauma as the leading cause of vertebral fractures, with falls accounting for more than half of the cases. Associated injuries were also present in more than half the patients, however, neurological deficit was uncommon. This highlights the importance of environmental health and safety, especially at the workplace and in public places. In contrast, the main cause in European and Chinese cohorts was road traffic accidents (36.08% of vertebral fracture-dislocations in the first[1] and 33.61% of spinal trauma in the second[2]). Associated injuries in European cases occurred at 45%, similar to the findings in this study.[1]

The conservative management employed in most patients possibly allowed for the short hospital stays observed. Those treated operatively stayed in hospital for an average of 12 days, which is higher than the mean length of hospital stay. However, this was not found to be statistically significant.

Operative management involves stabilizing the fracture through either a dorsal approach or, less commonly, a ventral approach. Surgery carried out dorsally is either a posterior fixation or an ultra-short posterior fixation. In the former the screws are inserted into the vertebrae above and below the fracture while in the latter, instrumentation is applied to the fractured vertebral body and the one above it only. The fourth operative option is a corpectomy, involving removal of the fractured vertebra and replacement with bone graft. This was not done on any patient in this cohort.

The AO system used to classify the fractures broadly separates fractures into three types, depending on the mechanism of injury. These are compression fractures (type A), distraction fractures (type B) and multidirectional with translation fractures (type C) and each category is further sub-classified.[3] In this study, the most prevalent fractures were type A, where the integrity of the bone and soft tissue structures is retained, possibly explaining how conservative management could be opted for to such an extent and why very few patient had neurological deficit.

The main limitation of this study is the small cohort involved because this made it difficult to prove any statistically significant correlation between length of hospital stay and other variables. However, it provides a valuable study tool to retrospectively investigate vertebral fractures. Also, the results shown above provide an insight into the characteristics of the patients affected and the causes and management trends of vertebral fractures.



THE STUDY IDENTIFIES TRAUMA AS THE LEADING CAUSE OF VERTEBRAL FRACTURES, WITH FALLS ACCOUNTING FOR MORE THAN HALF OF THE CASES

ACKNOWLEDGEMENTS

Mr Joseph N. Borg, consultant in orthopaedics and spinal surgery, who supervised the study, Dr Sascha Reiff, trainee in public health, who worked out the statistics, and Dr Edith Vassallo, trainee in radiology, who helped out in classifying the fractures.

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THE SLIPPERY SLOPE OF MODERN MEDICAL REPORTING – PART III

ALBERT CILIA-VINCENTI

With few exceptions, top scientists publish fewer, but much more important papers – Nobel Prize winners in physics, such as Albert Einstein or Richard Feynman are examples. Why keep repeating studies unless one is unhappy with their findings?

If one continually repeats studies, one is trying to get random chance to back them up, rather than letting science confirm their effectiveness. There may be 1000 studies showing a positive result and 950 showing a negative result, yet the "positives" are considered to prevail. Physicians often think this slight preponderance "proves it works".

The more studies performed, the greater the random chance of success when there should be failure. In medical statistics, studies are given a "statistical significance" rating, which is the level of confidence in the results. It answers the question: how much of the results are based on chance? A 95% confidence level is often used to show that a certain effect works, but also means there is a 5% probability that the result is due to chance alone – i.e., the "positive finding" would actually be false. A higher level of statistical significance raising confidence to 99% means much more money must be spent in the study, requiring more subjects, and also possibly entailing much more failure.

There have been about 15,000 fish oil studies based on 95% confidence level, meaning that 5% x 15,000 = 750 are truly failed studies which show positive results by pure chance. Therefore one should be wary of such enormous numbers of studies and that a negative finding is much stronger than a positive one.

When there is a desire to prove something, results are often incorrect or misinterpreted. This happens frequently in the nutritional field. Most of the recent more rigorously controlled studies prove fish oil doesn't work as claimed, reversing outdated 20th century findings. The latest is the failure of niacin to lower LDL cholesterol. Robert Giugliano of Harvard Medical School says that in a study of 25,000 people, niacin had not only no benefit, with no reductions in heart attack, stroke or death, but also showed higher risk of bleeding and new onset type 2 diabetes or diabetic complications.[1]

Do specific measurements really mean anything? For almost 50 years we have been led to believe that higher blood cholesterol levels accelerate atherosclerosis. Does this mean cholesterol itself is the problem, or is atherosclerosis actually caused by something else? There are now doubts whether lowering cholesterol with a drug automatically provides health benefits – as we'll see in future articles.

The influenza vaccine has been highly promoted as effective since 1946, but recently this vaccine has been reassessed. By 2020, US health leaders want 80% of the population to be vaccinated annually. This is a multibillion-dollar global business, but how good is the vaccine? Scientists at the Centre for Infectious Disease Research and Policy at the University of Minnesota recently claimed that the vaccine provides only modest protection for healthy young and middle-aged adults, and little if any protection for those over 65, who are most likely to succumb to the illness or its complications.[2] Moreover, the report's authors concluded that the expansion of vaccination recommendations was based on inadequate evidence and poorly executed studies. Michael T. Osterholm, director of both the Centre for Infectious Disease Research and Policy and of its Centre of Excellence for Influenza Research and Surveillance, states that "we have over-promoted and overhyped this vaccine. It does not protect as promoted. It's all a sales job and public relations". He continues, "I'm an insider. Until we started this project, I was one of the people out there heavily promoting it. It was only with this study that I looked and said, what are we doing?"

> ... "WE HAVE OVER-PROMOTED AND OVERHYPED THIS [INFLUENZA] VACCINE. IT DOES NOT PROTECT AS PROMOTED. IT'S ALL A SALES JOB AND PUBLIC RELATIONS."

Dr Osterholm said the authors discovered a recurring error in influenza vaccine studies that led to an exaggeration of the vaccine's effectiveness. They also discovered 30 inaccuracies in the statement on influenza vaccines put forth by the expert panel that develops vaccine recommendations, all of which favour the vaccine.

Medical researchers, just like professionals in other fields, are often highly motivated by status and rewards, and are often not objective. They can dogmatically defend an incorrect idea, even if they didn't originate it. Researchers linked to multi-billion industries are a particular risk to transparent correct science.

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NEW
The First Once-Daily Dual Bronchodilator[1]

THE FIRST ONCE-DAILY DUAL BRONCHODILATOR[1]

ULTIBRO® BREEZHALER®

START A NEW CHAPTER IN COPD[1-4]

Once-daily ULTIBRO BREEZHALER is indicated as maintenance bronchodilator treatment to relieve symptoms in adult patients with chronic obstructive pulmonary disease (COPD).[1]

Ultibro Breezhaler inhalation powder, hard capsules

▼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 6x1 or 30x1 hard capsules, together with one inhaler. **MARKETING AUTHORISATION HOLDER:** Novartis Europharm Limited, Frimley Business Park Camberley GU16 7SR, United Kingdom. **MARKETING AUTHORISATION NUMBERS:** EU/1/13/862/001 - EU/1/13/862/003. **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-26-JAN-2015

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NOVARTIS PHARMACEUTICALS

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LONG LIVE TO MALTA MEDICAL STUDENTS' ASSOCIATION (MMSA)

THE MOST ACTIVE STUDENT ORGANIZATION ON CAMPUS SINCE 1951!

GEORGIANA FARRUGIA
SECOND YEAR, MEDICAL STUDENT

The Malta Medical Students' Association (MMSA) has been accompanying me throughout my pre-clinical years, and it's what will continue to make the demanding med-school journey bearable. I still remember myself as a fresher. I was so keen on being a member of this association, consisting of a dedicated team of hard-working medical students, all sharing one altruistic aim: that of promoting good and improving the quality of life of everyone that comes across it.

Nowhere else but in this association have I seen so many outbursts of enthusiasm and genuine appreciation, which is what initially prompted me to volunteer, by providing free health checks to the general public in a variety of health-related events. Shortly after, I lent a helping hand by occupying the role of an *MMSA Official Photographer.* On top of this, last year I decided to take it a step further by joining the MMSA Publications team, as well as fulfilling the roles of *MMSA Teddy Bear Hospital Coordinator* during Summer 2014, and *MMSA International Coordinator* throughout the remaining academic period 2014/2015.

I simply cannot quantify how much I have gained from this association, for it has provided me with an environment in which I could thrive, both personally and professionally. It didn't take long before all this turned into a path of self-discovery. The MMSA has taught me more life lessons than any academic institution, but above all, I learnt to be flexible and open-minded. Now I feel more at ease when collaborating with a variety of individuals from different spectrums of life.

It is pretty understandable that with our busy lives as medical students it can be quite difficult to dedicate time to volunteering, but let me assure you, it's possible. And it is worth it. I encourage you to make the utmost of your University life, and start contributing to the success of our beloved MMSA. It is the same courage you need to touch other people's lives as a future physician.

THIS MONTH IN *medical history*

30 YEARS AGO

'2 Mar 1985' The US Food and Drug Administration (FDA) approved a screening test for HIV/AIDS, allowing contaminated blood to be excluded from blood transfusions

60 YEARS AGO

'11 Mar 1955' Death of Sir Alexander Fleming, Scottish bacteriologist. Joint winner of the 1945 Nobel Prize for Physiology or Medicine for discovering penicillin

200 YEARS AGO

'5 Mar 1815' Death of Franz Mesmer, German physician who developed mesmerism –considered by some to be the forerunner of modern hypnotism

TOP WEB READS THESYNAPSE.NET

1

DIATHERMY SMOKE EXTRACTION SHOULD BE COMPULSORY IN OPERATIONS

2

EXPOSURE TO MERCURY, SEAFOOD ASSOCIATED WITH RISK FACTOR FOR AUTOIMMUNE DISEASE

3

SEX HAS ANOTHER BENEFIT: IT MAKES HUMANS LESS PRONE TO DISEASE OVER TIME

THESYNAPSE

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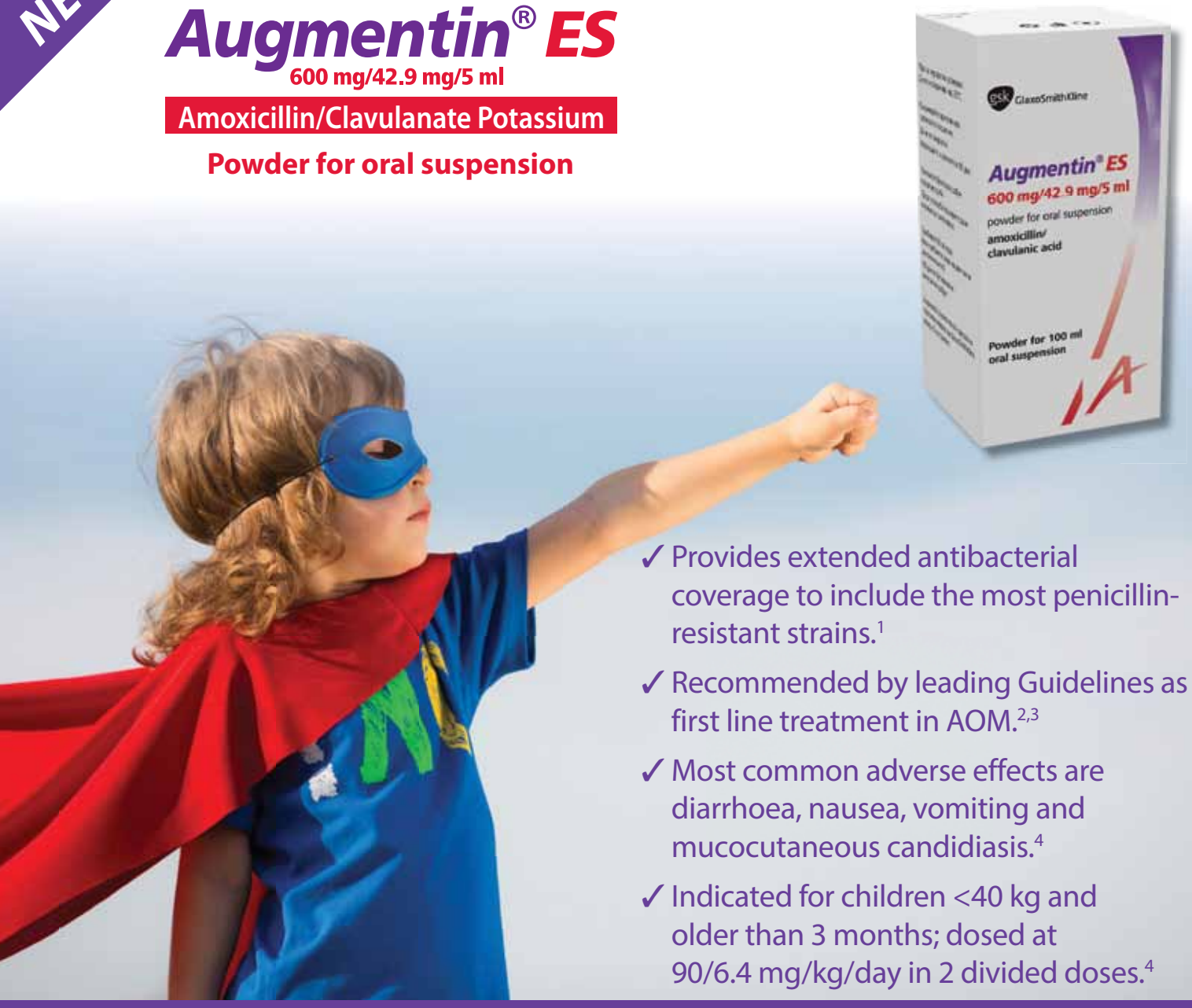
NEW

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.

Referneces:

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Job No: MLT_GIB/AES/0001/15

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COMPARATIVE STUDY OF THE FREQUENCY OF HYPERTENSION IN A PRIMARY CARE SETTING IN BUZA, TANZANIA & MALTA

ABSTRACT

Introduction: Worldwide prevalence of hypertension (HT) in established market economy countries is estimated at 37.4% for males and 37.2% for females.

Aim: To identify the frequency of HT in sample populations of Malta and Buza, Tanzania, looking specifically at gender differences, the rate of previous diagnosis and compliance to medication.

Methods: A comparative cross-sectional population-based survey to calculate the frequency of hypertension of a sample of the Maltese population reviewed in 2010 and a sample of people reviewed in a primary care medical clinic Buza in that same year. Both samples were statistically matched and compared.

Results: Frequency of HT in the Maltese sample was 32.8% (M:F - 32.8:32.8), and compliance rate was 48%. The frequency of HT in the Buza sample was 48.4% (M:F - 47.7:48.9) and the compliance rate was 8%. Frequency of stage II and malignant HT were significantly more prevalent in the Buza population. The frequency of HT increased with age in both populations studied.

Conclusions: Prevalence of examined HT in the Maltese sample was higher than the self-reported survey carried out in 2008, but still lower than the Buza sample and within range of the established market economy countries. Education and awareness of HT will increase lifestyle changes and further reduce the frequency of HT and increase the compliance rates in both populations. Hypertension awareness and readily available treatment is a much needed public health service. Furthermore, it is cheap, easy to offer and significantly improves quality of life.

KEY WORDS

Hypertension, age standardized prevalence, Malta, Tanzania

INTRODUCTION

Hypertension (HT) is defined by the World Health Organisation as a persistent raised arterial blood pressure (BP) of over 140/90 mm Hg. It is estimated that nearly one billion people have hypertension worldwide[1] and is one of the main risk factors for heart disease and stroke.[2] With an increasingly aging population, as well as rise of other risk factors such as obesity, HT is an ever-growing medical problem.

A recent systematic review on hypertension reports a worldwide prevalence of 37.4% in males and 37.2% in females in established market economy countries. The prevalence of HT varies greatly between countries, the lowest prevalence being in rural India (M:F-3.4:6.8%) and highest in Poland (M:F -68.9:72.5%). [3]

One multinational study carried out in the United States(US), Canada and six European countries (Germany, Finland, Sweden, England, Spain, Italy) reports the age- and sex-adjusted prevalence of HT to be 28% in the North American countries and significantly higher in the European countries (44%). [4]

A study reviewing compliance in the US reported 69% of the population to be aware of their HT diagnosis and the compliance rate to medication ranged from 53% to 79%. [5] The compliance rates in three Central European countries (Austria, Hungary, Slovakia) was found to be 53.5%.[6] A UK study reported a prevalence of 11.7% for the patient cohort 25-79 years and 46% for patients over 65 years. [7]

The Mediterranean country we intend to study is Malta. The population of Malta in 2009 was estimated to be 412,970 and is the eighth most densely populated country in the world (1,318 persons/km^2).[16] As a result of this high population density,92% of Malta is urban.[17] It has a GDP per capita of 19.248 billion US dollars.[18]

The EUROSTAT health interview survey conducted in 2008 shows the prevalence of hypertension in Malta to be 22.1%. It also reveals that 17.2% had been previously prescribed medication for their hypertension.[19]

We intend to compare the data from Malta to a suburb of Dar Es Salam, Tanzania, named Buza. Tanzania, an east African country, has a population of 38,329,000, and an estimated growth rate of 2%. The population distribution is uneven, varying from 1 person per sq. km to 134 per sq. km, to 1,787 per sq. km in Dar Es Salam. Over 80% of the population lives in rural areas.[20] GDP per capita stands at 1,416 US dollars.[21]

Hypertensive heart disease complications are shown to occur more frequently in Africans than in Europeans and North Americans and the majority of affected patients are younger. [22] This is a growing problem in all African communities[23]

A study carried out in Tanzania reported a prevalence rate of HT

Country study was carried out	Male Prevalence (%)	Female Prevalence (%)
India[3]	2.4	6.8
Girona, Spain[8]	14.1	16.9
South West of France[9]	21.0	19.0
Turkey[10]	31.8	31.6
Morocco[11]	30.2	37.0
Hellas, Greece[12]	33.8	28.4
Pavia, Italy[13]	40.0	19.0
Algeria[14]	32.7	44.0
San Marino[15]	44.0	47.0
Poland[3]	68.9	72.5

Table 1: Prevalence of Hypertension reported in different countries

in M:F- 30:26.8% in Ilala (urban area), and M:F - 32:31.5% in Shari (rural area). In both areas, less than 20% of hypertensive subjects were aware of their diagnosis and approximately 10% reported they had previously received treatment; less than 1% had controlled HT.[24] Another study carried out in an urban area in Tanzania reported a prevalence of 57% for type I HT and 30% for Type II HT.[25]

A similar trend in the prevalence of hypertension has been reported in other East African countries: Addis Ababa, Ethiopia M:F-31.5:28.9[26], Nakuru, Kenya 50.1%, comparable in men and women[27] and Mozambique; M:F - 35.7:31.2%.[28]

The aim of this study is to compare the prevalence of hypertension of Malta to Buza. We aim to compare the data whilst adjusting for age, gender and population size. To date we believe that this is the first comparative study to be done between these countries. The authors hypothesise that the prevalence of HT will be higher in Buza than in Malta due to an overall better quality of life in Malta (rank 28) compared to Tanzania (rank 109) on the Quality of Life Index scale[29]

METHODS

STUDY DESIGN

A comparative cross-sectional population-based survey to calculate the frequency of hypertension of a selected sample of the Maltese population compared to a sample of people reviewed in a primary care medical clinic Buza, Tanzania. Both samples were picked from an urban population setting, the latter population being of an overall lower socio-economic status.

SAMPLE POPULATION

The data for the sample of the Maltese islands was part of a national pilot study. This was conducted in 2010 as part of the European Health Examination Survey Pilot project. The Finnish lead partners developed the survey protocol. The Maltese team followed this protocol during the examination. Examinations were held in a public clinic in Gwardamangia, Malta and home visits were carried out where participants were unable to travel to clinic.

Using direct standardisation, the selected sample (n=400) was representative of the Maltese resident population aged 18 and over and selected randomly from an updated population register. Random stratification was conducted by gender, 10-year age group and region of residence.

Of the 221 participants, 219 (99.1%) had their blood pressure measured (for 2 participants the meeting never went ahead). 111 (50.7%) of the population were males, whilst 108 (49.3%) were females. Demographic data can be seen in table 2. The mean age of the population was 46years (range 18-86).

The protocol required that the blood pressure is measured three times. The average from the last two blood pressure measurements was taken as the final result. Apart from the measured data, respondents were asked before the examination if they have ever suffered from hypertension and if they were taking any medication for hypertension.

The **Buza sample** included any patient ≥ 18 years (n=202) who attended the clinic for any medical reason between the 19th July and 6th August 2010. Satisfactory data (in a few cases BP readings were not documented or taken by the clinician for one reason or other) was available on 198 patients (98.0%), 160 (85.0%) of whom were females and 38 (15%) were males. Demographic data can be seen in table 3. The mean age for the population studied was 37.8years. The ages ranged from 18 to 88 years.

In the **Buza** sample, every person attending the clinic had their blood pressure assessed by one of the clinicians. This was recorded in the patient's case notes (and repeated twice or more, so as to ensure accuracy), and then managed by the doctors working in the clinic.

Every patient attending the clinic had a full history taken by a doctor. Apart from the measured data, respondents were asked before the examination if they have ever suffered from hypertension and if they were taking any medication for hypertension.

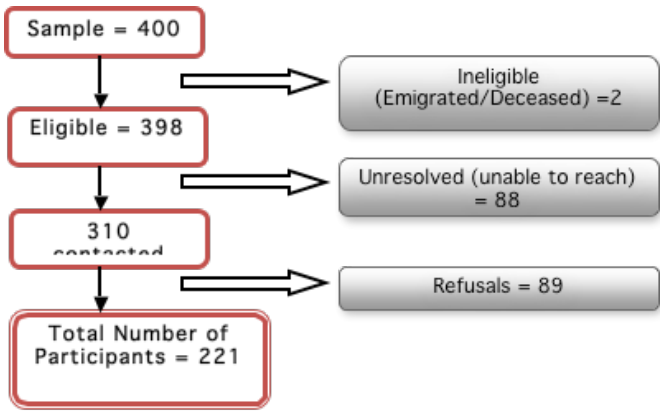

Figure 1: Sample of Maltese population

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 glycemic 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 in 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. If a dose of Galvus is missed, it should be taken as soon as the patient remembers. A double dose should not be taken on the same day. No dose adjustments are necessary 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. **WARNINGS / 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 ESRD on haemodialysis. 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 inconclusive. 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 (glyburide, 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 (≥1/3,000 to <1/1,000) angioedema, abnormal liver function tests, hepatic dysfunction (including hepatitis). 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. Combination with metformin: Common: tremor, headache, dizziness, nausea, hyperglycaemia, hyperhidrosis, asthenia. Uncommon: fatigue. Combination with sulphonylurea: Common: tremor, headache, dizziness, asthenia, hypoglycaemia. Uncommon: constipation. Very rare: osteoarthropathy. Combination with Thiazolidinediones: Common: weight increase, oedema peripheral, Uncommon: headache, asthenia, hypoglycaemia. Combination with insulin: Common: decreased blood glucose, headache, chills, nausea, gastro-oesophageal reflux disease. Uncommon: Diarrhoea, Rhinorrea. Frequency not known: urticaria, pancreatitis, hepatitis and abnormal liver function tests (reversible upon discontinuation of the medicinal product), bullous or exfoliative skin lesions. Combinations with metformin and a sulphonylurea: Common: hypoglycaemia, dizziness, tremor, hyperhidrosis, asthenia. **LEGAL CATEGORY: FOR PACK SIZES:** 7, 28 tablets **MARKETING AUTHORISATION HOLDER:** Novartis Europharm Limited, Frimley Business Park Camberley GU16 7SR United Kingdom. **MARKETING AUTHORISATION NUMBERS:** EU/1/07/414/001, 003. **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. 2014-MT- GAL-19-DEC-2014

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, indicated in the treatment of adult 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 individualised 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 tablet 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 with metformin and a sulphonylurea: The doses 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 dosed as 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 more information. 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 precoma. Renal failure or renal dysfunction defined as creatinine clearance < 60 ml/min. Acute conditions with the potential to affect 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 could be monitored at least once yearly 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. LFT's 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 3x ULN or greater persist, withdrawal of Eucreas therapy is recommended. Patients who develop jaundice or other signs suggestive of liver dysfunction should discontinue Eucreas. Routine monitoring of diabetic patients for skin disorders such as blistering or ulceration is recommended. As Eucreas contains metformin, treatment should be discontinued 48 hours before elective surgery with general anaesthesia and not usually resumed earlier than 48 hours afterwards. The IV 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 (glyburide, pioglitazone, metformin), amlodipine, digoxin, ramipril, simvastatin, valsartan or warfarin were observed after co-administration with Vildagliptin. Interactions with Metformin hydrochloride that are not recommended include alcohol, cationic active substances e.g. cimetidine and intravascular administration of iodinated contrast media. Combinations requiring caution include metformin hydrochloride with medicines binding to produce hyperglycaemic activity e.g. glucocorticoids, beta agonists and diuretics. The dose of antihyperglycaemic medicinal products may need to be adjusted in combination with ACE inhibitors. **ADVERSE REACTIONS:** Rare cases (≥1/3,000 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, hyperglycaemia. Uncommon: fatigue. Combination with Metformin and sulphonylurea: Common: hypoglycaemia, dizziness, tremor, hyperhidrosis, asthenia, decreased blood glucose, headache, chills. Combination with insulin: Decreased blood glucose, headache, chills, nausea, gastro-oesophageal reflux disease, diarrhoea, Rhinorrea. For a full list of Adverse reactions, please refer to the SmPC. **LEGAL CATEGORY:POM PACK SIZES:** 30, 60 filmcoated tablets **MARKETING AUTHORISATION HOLDER:** Novartis Europharm Limited, Wimblehurst Road, Horsham, West Sussex, RH12 5AB, United Kingdom. **MARKETING AUTHORISATION NUMBER:** EU/1/07/425/002–003, EU/1/07/425/008-009. **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. 2014-MT-EUC-09-JUN-2014

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NOVARTIS PHARMACEUTICALS

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

Galvus vildagliptin

Eucreas vildagliptin/metformin

		Male % (N)	Female % (N)	Total % (N)
Total		**50.7 (111)**	**49.3 (108)**	**100 (219)**
Age	<25	9 (10)	8.3 (9)	8.7 (19)
	25 – 34	19.8 (22)	16.7 (18)	18.3 (40)
	35 – 44	15.3 (17)	13.9 (15)	14.6 (32)
	45 – 54	15.3 (17)	18.5 (20)	16.9 (37)
	55 – 64	22.5 (25)	24.1 (26)	23.3 (51)
	65 – 74	13.5 (15)	12 (13)	12.8 (28)
	75+	4.5 (5)	6.5 (7)	5.5 (12)

Table 2: Overview of age frequency of the Maltese sample

		Male % (N)	Female % (N)	Total % (N)
Total		**19.2 (38)**	**80.8 (160)**	**100 (198)**
Age	<25	13.2 (5)	8.8 (14)	9.6 (19)
	25 – 34	18.4 (7)	28.1 (45)	26.3 (52)
	35 – 44	5.3 (2)	22.5 (36)	19.2 (38)
	45 – 54	13.2 (5)	18.1 (29)	17.2 (34)
	55 – 64	21.1 (8)	10 (16)	12.1 (24)
	65 – 74	23.7 (9)	8.1 (13)	11.1 (22)
	75+	5.3 (2)	4.4 (7)	4.5 (9)

Table 3: Overview of age frequency of the Buza sample

INCLUSION CRITERIA

The sample from both populations included any adult ≥ 18 years of any gender and social class. Only participants who could give informed consent were included in this study.

EXCLUSION CRITERIA

All patients under the age of 18 years were excluded from our study.

ETHICAL CONSIDERATIONS

Participation in both surveys was against informed consent. All participants were asked to consent to the anthropometric measures separately from other components of the examination such that they could chose to opt out of specific measures without being excluded from the examination. Only participants who were deemed to have capacity to consent to the study at that present time were included. The final dataset was anonymized and kept confidential using password protected datasets.

DATA ANALYSIS

All data collected was inputted into Microsoft Excel and analysed using SPSS version 19. The Buza and Maltese sample were split by age and gender and Fisher's Exact test was used to see how comparable the study populations were. While there were no significant differences between the male populations (Malta n=111, Buza n= 38, P=0.58) there was a significant difference between the female populations (Malta n= 108, Buza n=160, p< 0.001). Also the Buza population had a gender imbalance within their sample i.e. an overly high proportion of females; whilst the Maltese sample had a higher proportion of persons aged 55-64 years when compared to the national population. These sample differences made it difficult to compare populations, so direct standardisation was used to calculate age-standardised prevalence against the resident Maltese population in 2009. Confidence intervals were then calculated.

RESULTS

PREVALENCE

The age standardised rate of HT in the Maltese population was 32.8%, 95% confidence intervals 95% +/-5.1% (95% CI). This was statistically significantly lower than the age standardised rates of HT for the population in Buza i.e. 48.4% (95%CI+/-6.5%).

The standardised rates for males in Malta (32.9%, 95%CI +/- 7.8%) were lower than the Buza male sample (47.7%, 95%CI +/- 16.8%). A similar trend was seen in the female sample; the frequency in Malta was 32.9% (95%CI +/- 6.3%) compared to the Buza sample 48.9% (95% CI +/- 7.6%).

STAGES OF HYPERTENSION

A blood pressure within normal range was found in 73 cases (33.3%) of the Maltese population, which was slightly lower than the population studied in Buza (n=69, 34.3%). There was a higher proportion of the Maltese population who presented in a pre-hypertensive stage (n=72, 32.9%) compared to Buza (n=43, 21.7%). Stage 1 hypertension was commoner in the Malta sample (n=54, 24.7%) when compared to the Buza sample (n=25, 12.6%). However, there was a markedly higher frequency of stage 2 hypertension recorded in the Buza sample (n= 31, 15.7%).

INCIDENCE AND CONTROLLED CASES

62 cases in the Buza sample (69.7%, CI 95% 60.1 – 74.2%) were incident cases. The frequency of new cases was higher than the Maltese sample (n=38, 51.1%).

48 cases were prescribed medication in the Maltese sample; 23 (47.9%) of these patients had their hypertension controlled (i.e. blood pressure < 140/90mmHg). The rate of controlled hypertension was significantly higher (P<0.001) than the number of cases in the Buza sample (n=2), out of 25 patients meant to be on medication.

DISCUSSION

The prevalence of HT in the Maltese sample was lower (32.8%) than the sample studied in Buza (48.5%). However the frequency was higher than the self-reported survey (22.5%) carried by the department of health in 2008. This result of examined blood pressure is more reliable than the self-reported results carried out in 2008. The above result is in keeping with the authors' hypothesis and can probably be explained by the substantial difference in the quality of life between the two countries (Malta 28th and Tanzania 109th).

The prevalence in Malta was lower than the average calculated for the market economy countries (37.3%) and North Africa Mediterranean countries (Algeria and Morocco), similar to the prevalence reported in Greece and Turkey but higher than the western European countries (Spain and South West France).[3] The prevalence in Buza was found to be within the range reported in studies (30-57%) carried out previously in Tanzania.[24,25] The prevalence in Buza was higher than that reported in Ethiopia (31%)[26] and Mozambique (33.5%)[28], but lower than that found in Nakuru, Kenya (50.1%).[27]

No statistically significant difference was found between males and females in both population samples. The prevalence of patients suffering from Stage 2 Hypertension in Buza (12.6%) was more than double that of Malta (5.9%). However the Maltese sample had a higher prevalence of patients with Stage 1 Hypertension and Pre-Hypertensive blood pressure. Malta also had a higher prevalence rate but a lower incidence rate than Buza, highlighting the greater awareness and availability of clinics to manage HT in Malta and other developed nations.

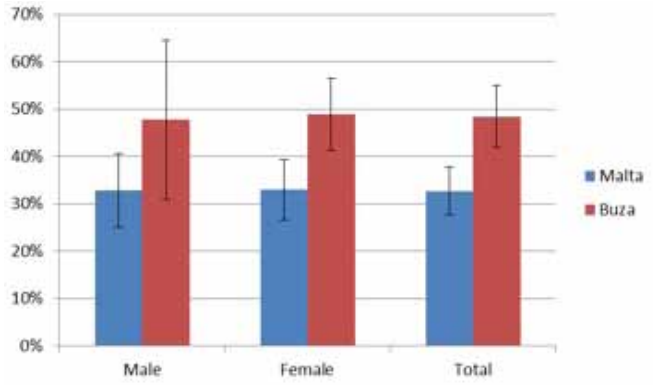

Figure 2: Frequency of hypertension by gender

	Malta *N (%)*	Buza *N (%)*
Total Cases	**74 (100)**	**88 (100)**
Incidence	38 (51.4)	62 (69.7)
Prevalence	36 (48.6)	27 (30.3)
Prescribed medication	48 (64.8)	25 (28.4)
No prescribed medication	26 (35.1)	63 (71.6)

Table 5: Comparisons between Malta and Tanzania for incidence and medication

It was also found that in both hypertensive cohorts, the Maltese patients had better HT control. This reflects a better compliance rate amongst the Maltese population (48% compared to 8% in Buza) which may be related to a greater HT awareness amongst the population and healthcare professionals in Malta. This could also be a result of more widely available health services. Less than a third of the sample in Buza were aware that they were suffering from high blood pressure; this is comparable to a parallel study (20%) carried out in Ilalia Tanzania.[24] Over 9% of the target population in Buza had malignant hypertension, but no cases of malignant hypertension were reported in Malta, further substantiating better HT awareness and the availability of services.

It was further observed that in the 35-44 and 45-54 year age groups the prevalence of hypertension in women in Buza rose from 33% to 66%. One can hypothesise that most probably almost all women in menopause were suffering from hypertension. This is further substantiated by the increase in frequency of hypertension with age. In males this increase in HT was not statistically significant (P = 0.149) though this could be a result of the small male sample. This finding differs from other studies as the rate of HT in males increases proportionally with age.[30] The trend of proportionally increasing

	Malta *N (%, 95%CI)*	Buza *N (%, 95%CI)*
Total	**219 (100)**	**198 (100)**
Blood pressure within normal range	73 (33.3, 39.5 – 27.1)	68 (34.3, 43.7 – 25.1)
Pre-hypertensive: 120-139/80-89	72 (32.6, 38.8 – 26.4)	43 (21.7, 29.3 – 13.6)
Stage 1 hypertension:140-159 or >90-99	54 (24.4, 30.1 – 18.7)	31 (15.7, 22.8 – 8.6)
Stage 2 hypertension: >160/100	13 (5.9, 9.0 – 2.8)	25 (12.6, 19.1 – 6.1)
Malignant hypertension:>180/110	0 (0)	19 (9.6, 15.4 – 3.8)
Hypertension >130/80 with DM, CHD,MI, CVA, kidney disease	6 (2.7, 4.8 – 0.6)	6 (3, 6.3 – 0.6)
Isolated hypertension:>140 and<90	1 (0.5, 1.4 – 0.4)	6 (3, 6.3 – 0.6)

Table 4: Number of cases in the different stages of hypertension

New

TRIPLIXAM®

perindopril / indapamide / amlodipine

Triple-drug combination in hypertension

- The power to reduce and control blood pressure[1]
- The power of an excellent compliance[1]
- The power to reduce mortality[2]

1 TABLET DAILY

COMPOSITION: Triplixam 5mg/1.25mg/5mg film-coated tablets 5 mg perindopril arginine (per)/1.25 mg indapamide (ind)/5 mg of amlodipine (amlo); Triplixam 10mg/2.5mg/5mg film-coated tablets: 10 mg per/2.5 mg ind/5mg amlo; INDICATIONS: Substitution therapy for treatment of essential hypertension, in patients already controlled with perindopril/indapamide fixed dose combination and amlodipine, taken at the same dose level. DOSAGE AND ADMINISTRATION: One tablet per day, preferably in the morning and before a meal. The fixed dose combination is not suitable for initial therapy. If a change of the posology is required, titration should be done with the individual components. Paediatric population: should not be used. CONTRAINDICATIONS: Dialysis patients. Patients with untreated decompensated heart failure. Severe renal impairment (Clcr < 30 mL/min). Moderate renal impairment (Clcr 30-60 mL/min) for Triplixam 10mg/2.5mg/5mg and 10mg/2.5mg/10mg. Hypersensitivity to the active substances, to other sulphonamides, to dihydropyridine derivatives, any other ACE-inhibitor or to any of the excipients. History of angioedema (Quincke's oedema) associated with previous ACE inhibitor therapy. Hereditary/idiopathic angioedema. Second and third trimesters of pregnancy (see Warnings and Pregnancy and lactation sections). Lactation (see Pregnancy and lactation section). Hepatic encephalopathy. Severe hepatic impairment. Hypokalaemia. Severe hypotension. Shock, including cardiogenic shock. Obstruction of the outflow-tract of the left ventricle (e.g. high grade aortic stenosis). Haemodynamically unstable heart failure after acute myocardial infarction. Concomitant use with aliskiren in patients with diabetes mellitus or renal impairment (GFR < 60mL/min/1.73m2) (see Warnings and Interaction(s) sections). WARNINGS: Special warnings: Neutropenia/agranulocytosis/thrombocytopenia/ anaemia: caution if collagen vascular disease, immunosuppressant therapy, treatment with allopurinol or procainamide, or combination of these complicating factors, especially if pre-existing impaired renal function. Monitoring of white blood cell counts. Hypersensitivity/angioedema, intestinal angioedema: stop treatment and monitor until complete resolution of symptoms. Anaphylactoid reactions during desensitization: Caution in allergic patients treated with desensitization and avoid if venom immunotherapy. Temporarily withdrawal of ACE-inhibitor at least 24 hours before desensitization. Anaphylactoid reactions during LDL apheresis: Temporarily withholding ACEinhibitor prior to each apheresis. Haemodialysis patients: consideration to use a different type of dialysis membrane or class of antihypertensive agent. Pregnancy: no initiation during pregnancy, stop treatment and start alternative therapy if appropriate. Hepatic encephalopathy: stop treatment. Photosensitivity: stop treatment. Precautions for use: Renal function: In certain hypertensive patients without pre-existing apparent renal lesions and for whom renal blood tests show renal insufficiency, stop treatment and restart at a low dose or with one constituent only. Monitoring of potassium and creatinine, after two weeks of treatment and then every two months during therapeutic stability period. If bilateral renal artery stenosis or single functioning kidney: not recommended. Risk of arterial hypotension and/or renal insufficiency (in cases of cardiac insufficiency, water and electrolyte depletion, in patients with low blood pressure, renal artery stenosis, congestive heart failure or cirrhosis with oedema and ascites): start treatment at low doses and increase progressively. Hypotension and water and sodium depletion: Risk of sudden hypotension in presence of pre-existing sodium depletion (in particular if renal artery stenosis): Monitoring of plasma electrolytes, re-establish blood volume and pressure, restart treatment at a reduced dose or with only one of the constituents. Sodium levels: More frequent monitoring in elderly and cirrhotic patients. Potassium levels: Hyperkalaemia: Monitoring of serum potassium if renal insufficiency, worsening of renal function, age (> 70 years), diabetes mellitus, intercurrent events, in particular dehydration, acute cardiac decompensation, metabolic acidosis and concomitant use of potassium-sparing diuretics, potassium supplements or potassium salts, or other drugs associated with increases in serum potassium. Hypokalaemia: risk for elderly and/or malnourished subjects, cirrhotic patients with oedema and ascites, coronary patients, patients with renal failure or heart failure, long QT interval: monitoring of serum potassium. Calcium levels: hypercalcemia: stop treatment before investigating the parathyroid function. Renovascular hypertension: if renal artery stenosis: start treatment at hospital at low dose; monitor renal function and potassium. Dry cough. Atherosclerosis: start treatment at low dose in patients with ischaemic heart disease or cerebral circulatory insufficiency. Hypertensive crisis. Cardiac failure/severe cardiac insufficiency: Caution if heart failure. Severe cardiac insufficiency (grade IV): start treatment under medical supervision with reduced initial dose. Aortic or mitral valve stenosis / hypertrophic cardiomyopathy: Caution if obstruction in the outflow tract of the left ventricle. Diabetic patients: If insulin dependent diabetes mellitus, start treatment under medical supervision with reduced initial dose; monitor blood glucose during the first month and/or in the case of hypokalaemia. Black people: higher incidence of angioedema and apparently less effective in lowering blood pressure than in non-blacks. Surgery / anaesthesia: stop treatment one day before surgery. Hepatic imparment: Mild to moderate: caution. Stop treatment if jaundice or marked elevations of hepatic enzymes. Uric acid: hyperuricemia: Increased tendency to gout attacks. Older people: testing of renal function and potassium levels before treatment start. Dosage increase with care. INTERACTION(S): Contraindicated: Aliskiren in diabetic or impaired renal patients. Not recommended: Lithium, Aliskiren in patients other than diabetic or impaired renal patients, Concomitant therapy with ACE inhibitor and angiotensin-receptor blocker, Estramustine, Potassium-sparing drugs (e.g triamterene,amiloride,...), Potassium salts, Dantrolene (infusion), Grapefruit or grapefruit juice. Special care: Baclofen, Non-steroidal anti-inflammatory medicinal products (included acetylsalicylic acid at high doses), Antidiabetic agents (insulin, hypoglycaemic agents), Non-potassium-sparing diuretics and Potassium-sparing diuretics (eplerenone, spironolactone), Torsades de pointes inducing drugs, Amphotericin B (IV route), glucocorticoids and mineralocorticoids (systemic route), tetracosactide, stimulant laxatives, Cardiac glycosides, CYP3A4 inducers, CYP3A4 inhibitors. To be taken into consideration: Imipramine-like antidepressants (tricyclics), neuroleptics, other antihypertensive agents and vasodilatators, tetracosactide, Allopurinol, cytostatic or immunosuppressive agents, systemic corticosteroids or procainamide, Anaesthetic drugs, Diuretics (thiazide or loop diuretics), Gliptines (linagliptine, saxagliptine, sitagliptine, vidagliptine), Sympathomimetics, Gold, Metformin, Iodinated contrast media, Calcium (salts), Ciclosporin, Atorvastatin, digoxin, warfarin or ciclosporin, Simvastatin. PREGNANCY AND BREASTFEEDING: Not recommended during the first trimester of pregnancy. Contraindicated during the second and third trimesters of pregnancy and lactation. FERTILITY: Reversible biochemical changes of spermatozoa in some patients treated by calcium channel blockers. DRIVE & USE MACHINES: May be impaired due to low blood pressure that may occur in some patients, especially at the start of treatment. UNDESIRABLE EFFECTS: Common: dizziness, headache, paresthesia, vertigo, somnolence,
dysgeusia, visual disturbances, tinnitus, palpitations, flushing, hypotension (and effects related to hypotension), cough, dyspnoea, abdominal pain, constipation, diarrhea, dyspepsia, nausea, vomiting, pruritus, rash, maculopapular rashes, muscle cramps, ankle swelling, asthenia, fatigue, oedema. Uncommon: eosinophilia, hypoglycaemia, hyperkalaemia reversible on discontinuation, hyponatraemia, insomnia, mood changes (including anxiety), mood disturbances, depression, sleep disorder, hypoesthaesia, tremor, syncope, diplopia, tachycardia, vasculitis, bronchospasm, rhinitis, dry mouth, altered bowel habits, urticaria, angioedema, hypersensitivity reactions, mainly dermatological, in subjects with a predisposition to allergic and asthmatic reactions, alopecia, purpura, skin discoloration, hyperhidrosis, exanthema, photosensitivity reactions, pemphigoid, arthralgia, myalgia, back pain, micturition disorder, nocturia, increased urinary frequency, renal failure, erectile dysfunction, gynaecomastia, pain, chest pain, malaise, oedema peripheral, pyrexia, weight increase, weight decrease, blood urea increased, blood creatinine increased, fall. Rare: confusion, blood bilirubin increased, hepatic enzyme increased. Very rare: agranulocytosis, aplastic anaemia, pancytopenia, haemoglobin decreased and haematocrit decreased, leucopenia, neutroperia, haemolytic anaemia, thrombocytopenia, allergic reactions, hyperglycaemia, hypercalcaemia, hypertonia, peripheral neuropathy, angina pectoris, arrhythmia (including bradycardia, ventricular tachycardia and atrial fibrillation), myocardial infarction, possibly secondary to excessive hypotension in high risk patients, stroke possibly secondary to excessive hypotension in high-risk patients, eosinophilic pneumonia, gingival hyperplasia, pancreatitis, gastritis, hepatitis, jaundice, abnormal hepatic function, erythema multiform, Stevens-Johnson Syndrome, exfoliative dermatitis, toxic epidermic necrolysis, Quincke's oedema, acute renal failure. Not known: Potassium depletion with hypokalaemia, particularly serious in certain high risk populations, torsades de pointes (potentially fatal), possibility of onset of hepatic encephalopathy in case of hepatic insufficiency, possible worsening of pre-existing acute disseminated lupus erythematosus, electrocardiogram QT prolonged, blood glucose increased, blood uric acid increased. OVERDOSE. PROPERTIES: Perindopril is an inhibitor of the angiotensin converting enzyme (ACE inhibitor) which converts angiotensin I to angiotensin II. Indapamide is a sulphonamide derivative with an indole ring, pharmacologically related to the thiazide group of diuretics. Amlodipine is a calcium ion influx inhibitor of the dihydropyridine group (slow channel blocker or calcium ion antagonist) and inhibits the transmembrane influx of calcium ions into cardiac and vascular smooth muscle. PRESENTATION: Box of 30 tablets of Triplixam 5mg/1.25mg/5mg, and 10mg/2.5mg/5mg. LES LABORATOIRES SERVIER, 50 rue Carnot, 92284 Suresnes cedex France. www.servier.com For complete information, please refer to the Summary of Product Characteristics

1.Toth K, on behalf eg the PIANIST Investigators. Am J Cardiovasc Drug 2014;14:137-145
2.Chalmers J, et al. Hypertension 2013;63:259-264

HT in both sexes by age was found in the Maltese sample. The greater frequency of HT in Malta may be a result of Malta's ageing population, with 13% of the population above the age of 65.

STRENGTHS AND LIMITATIONS OF THE STUDY

The results from our study report only examined BP as opposed to self-reporting, thus reducing a recall bias.

The population sample in this study did not only include patients who were ill but also those who attended the clinic merely for a check up, thus reducing the selection bias.

All patients had their BP checked at least twice in keeping with recommended standards.

Limitations of this study include a relatively small sample size, although direct standardisation was used to account for any discrepancies in representation of the target population. A longitudinal study with a larger sample size is recommended.

CLINICAL IMPLICATIONS

In keeping with the human development index, the prevalence of HT in the Maltese sample was lower than that found in the Buza sample. Further education and awareness campaigns directed to all ages of the population on HT prevention strategies would reduce prevalence rates in the Maltese population and also improve the HT medication compliance rates.

The prevalence of hypertension is expected to rise substantially in sub-Saharan Africa, so the authors call for population-based studies and registries of the epidemiology of hypertension in the African population. The provision of awareness campaigns and more clinics available for assessment and management of HT in the health services in Tanzania is strongly recommended. As reported in this study this cheap provision of service yields quick positive results, thus improving the overall quality of life of the people living in Tanzania.

As other HT studies reported in other countries, more than half of respondents took action following the receipt of advice.[5] The authors believe that this simple measure will have a highly positive effect on the people living in these countries.

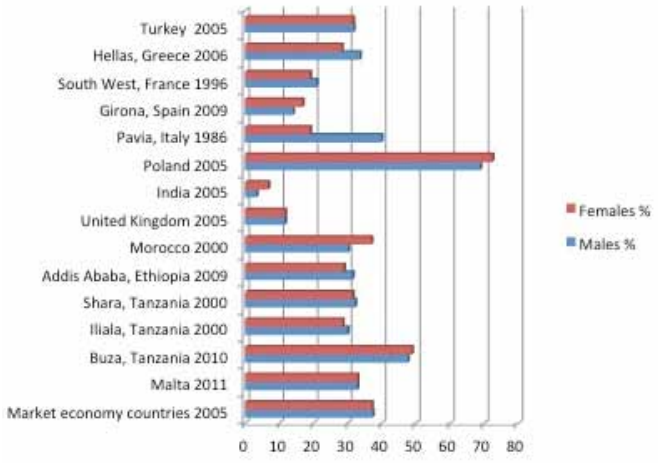

Figure 3: Male and female prevalence of hypertension

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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 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, Gzira GZR 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]

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

Theravance | gsk

MARIKA AZZOPARDI

BEING A PHARMACIST BY PROFESSION GENERALLY MEANS BEING COOPED UP INDOORS FOR ALL YOUR WORKING HOURS, FACING SICK CLIENTS REQUIRING MEDICINALS AND DISPENSING ADVICE. BUT MANY PHARMACISTS TEND TO HAVE ANOTHER SIDE TO THEIR LIFE, ONE WHICH GENERALLY TAKES THEM PLACES AND BRINGS THEM IN CONTACT WITH THE GREAT OUTDOORS IN VERY SPECIFIC MANNERS.

PHARMACIST PHOTOGRAPHER

Franklin Camilleri is a case in point. A pharmacist since 1992, he was always in public service rather than being a full-time dispensing pharmacist, and he gradually moved up the ranks of diverse departments and gained expertise in his sector of specialisation. Today he works at the government's Central Procurement and Supplies Unit (CPSU) wherein he holds a post of great responsibility as Principal Pharmacist within the Emergency Response Unit (ERU). His work not only involves meticulously scouring the government medicinal supplies and providing options to fill gaps according to need, but also a great deal of office work, delegation and coordination. This involves dealing with local and foreign pharmaceutical supply agencies, different shipping couriers and agencies as well as all the local public hospitals and health clinics. Nowadays with the setting up of the POYC system, his involvement with this part of the market is very intense. The work also involves a good level of research into product development and the carrying out of evaluations of medicine costs, which tasks are regularly required especially when certain stocks run low and replacement products must be procured as speedily as possible.

Ghajn Tuffieha

> "We currently have 60+ items considered as fast movers within the POYC system and these include products such as aspirin - all must be constantly in supply. All medicinals are imported into Malta and when there is a shortage of a raw material that composes a specific product, the sourcing company is the first to stop supply. It is understandable that no raw materials translates in manufacturing problems and supply discrepancies. Moreover, once a manufacturer detects the possibility of an extraordinary or emergency demand in his own country or region, exports are the first to get blocked since all products are retained for local use. For instance, blood products are quickly retained by warring countries or countries which are on the brink of civil strife."

But all this indoor work gives scope to a passion for something totally creative and this 44-year-old gentleman is an amateur photographer close to turning professional. He claims he became addicted to photography, most especially when the digital era came into fashion. "I had always been

Cappadocia

Nature

fascinated by photography and still have the first important camera I purchased in the 1980s, but in the past this hobby necessitated a great deal of technical know-how, dark-room development skills and the like. It was somewhat more complicated. Once digital photography became available, I had no qualms about embracing the hobby with eagerness. Naturally I have taken several courses and attended workshops to learn more about photography because you never know enough and I pay special attention to the techniques I use and effects I manage to achieve."

Today, he likes to photograph landscapes, seascapes, scenery in general. Sometimes friends and family ask him to photograph special events or to take portraits. Franklin travels a lot with like-minded friends, specifically to take pictures, many of which are carefully examined, refined and filed for future use. "I would love to exhibit my works one day but still feel I am not prepared, although all those who see my photographs say to the contrary."

QUIZ

WHICH NOVEL BACTERIA HAS BEEN HAILED IN THE EDITORIAL AS THE SOURCE OF A POSSIBLE WONDER DRUG, TEIXOBACTIN?

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QUIZ WINNER

WINNER OF THE MEDICAL LANGUAGE TRANSLATOR BOOK PUBLISHED BY MMSA

CHARMAINE ZAHRA 4TH YEAR MEDICAL STUDENT, IS THE LUCKY WINNER OF THE MEDICAL LANGUAGE TRANSLATOR BOOK PUBLISHED BY MMSA. SHE WAS THE 5TH PARTICIPANT WHO REPLIED CORRECTLY TO THE QUESTION, 'IN THIS ISSUE WE HAVE UK-BASED CONTRIBUTORS AS WELL AS AN AUSTRALIA-BASED CONTRIBUTOR. IDENTIFY ONE OF THESE CONTRIBUTORS.' THE CORRECT ANSWERS WERE DR ALEXANDER BORG, MR JOHN CASALETTO & PROF. MAURICE CAUCHI.

PIERRE VASSALLO

IMAGING HAMSTRING MUSCLE INJURIES

Hamstring muscle injuries (HMI) are the most commonly encountered sports-related injuries. There are also often quite difficult to treat. The aim of imaging such injuries is to provide an estimate of the nature and extent of the injury, which would guide treatment (conservative or surgical) and minimize unnecessary and often detrimental convalescence. Minimizing the duration of inactivity is not only important in professional athletes, but also in generally active individuals who enjoy sport for leisure.

The typical history of an HMI is sudden severe pain located in the posterior aspect of the thigh that usually stops further participation in the sporting activity. Not all pain in the posterior aspect of thigh is due to HMI; sciatic nerve root impingement and sacroiliac joint disease may result in a similar pain pattern.

The hamstring muscle group consists of three muscles: the biceps femoris, semitendinosus and semimembranosus muscles (Fig. 1).

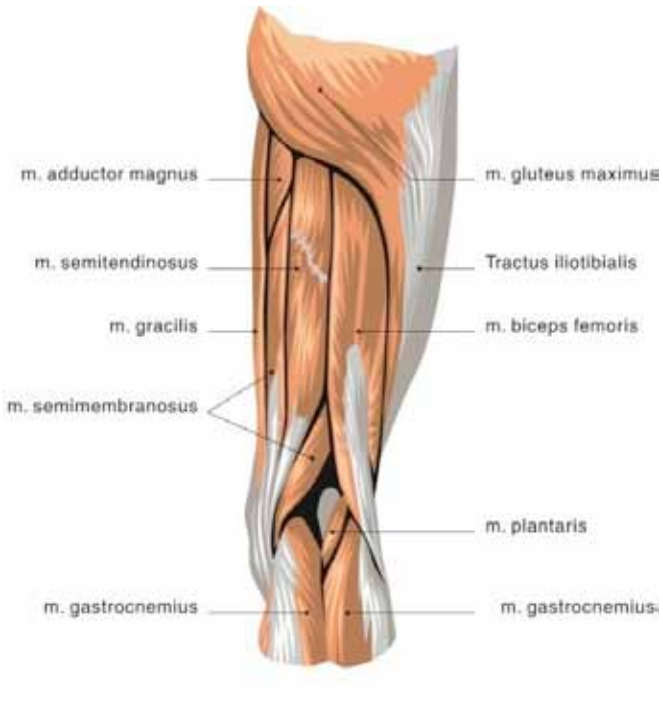


Fig 1: Anatomy of the hamstring muscles.

The biceps femoris muscle has two heads (hence the name), the long head which attaches to the medial facet of the ischial tuberosity and the short head which attaches to the posterior aspect of the femur. The biceps femoris inserts distally into the head of the fibula, the lateral condyle of the tibia and the lateral fascia of the leg. Each of the two components of the biceps femoris has a different nerve supply, which may result in incoordination, a factor that has been attributed to its increased predisposition for injuries.

The semitendinosus muscle origin inserts in common with the long head of biceps into the ischial tuberosity (known as the conjoint tendon). It has a central raphe with superior and inferior muscle components and inserts distally in the postero-medial aspect of the tibia (Gerdy's tubercle).

The semimembranosus muscle arises from the supero-lateral aspect of the ischial tuberosity, separate from the remaining hamstring muscle, and has a complex distal insertion composed of 5 variable bands, which attach to the medial aspect of the tibia,

the adjacent knee joint capsule and associated posterior oblique and acruate ligaments. An additional variable attachment to the posterior horn of the medial meniscus may also be observed.

Since most of the components of the hamstring muscles cross two joints, the degree of stretching and tensile strength in these muscles is greater than muscles that cross single joints. The hamstring muscles are also mostly composed of Type 2 fibres, which have high tensile contractions and strength and are hence more prone to injury. Injures most commonly occur at the musculo-tendonous junction (MTJ), which is a 10-12cm transition zone that correlates with the transition of the myofibrils from the muscle into the tendon. Injuries may be of various degrees of severity, from a muscle ache that results from vigorous muscle exercise, through minor, moderate and severe strain to a complete tear. All forms of injury are related to a disruption of the myofibrils with resultant accumulation of extracellular fluid, which may be so minor that it is not detected on imaging studies. More severe degrees of myofibrillar disruption result in visible accumulation of extracellular fluid in the form of oedema. In the acute phase, haemorrhage may also be present at the site of injury. Subsequently, repair of the injury is through the laying down of fibrous tissue (scar), which may appear as early as 14 days after injury. Although scar tissue has considerable tensile strength, it results in shortening of the muscle as well as decreased muscle elasticity, both of which increase the risk of a future tear.

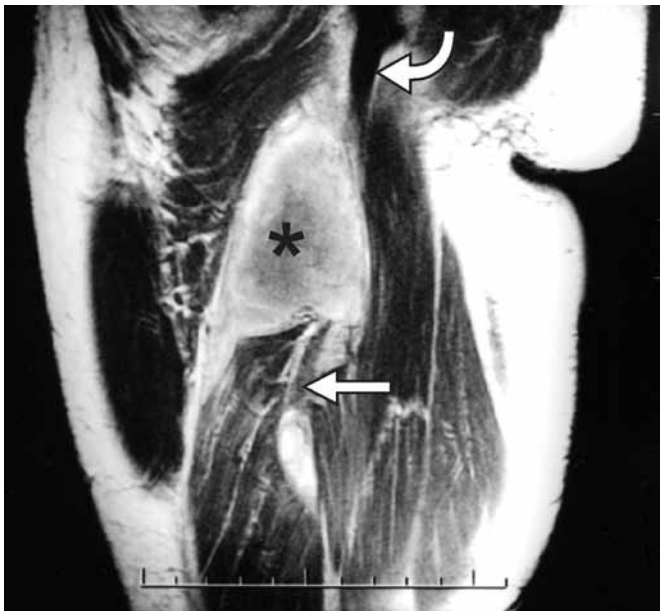


Fig 2: Proximal avulsion injury of the hamstring muscles. Oblique coronal T1-weighted MR image demonstrates a large hematoma (*) with retracted fibres of the semitendinosus muscle and the long head of the biceps femoris tendon (straight arrow). The semimembranosus muscle (curved arrow) is intact.

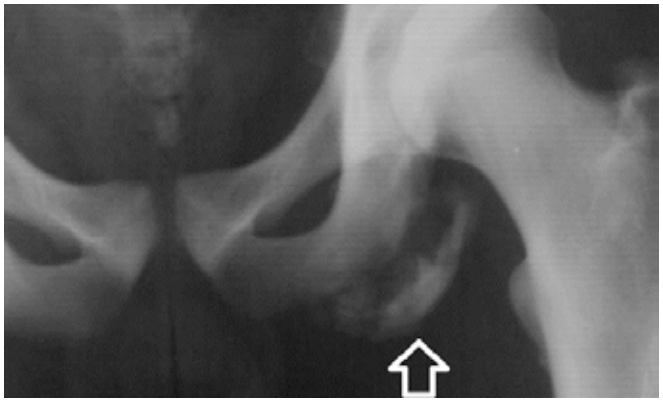


Fig 3: Bony avulsion (arrow) of the hamstring insertion seen on X-ray.

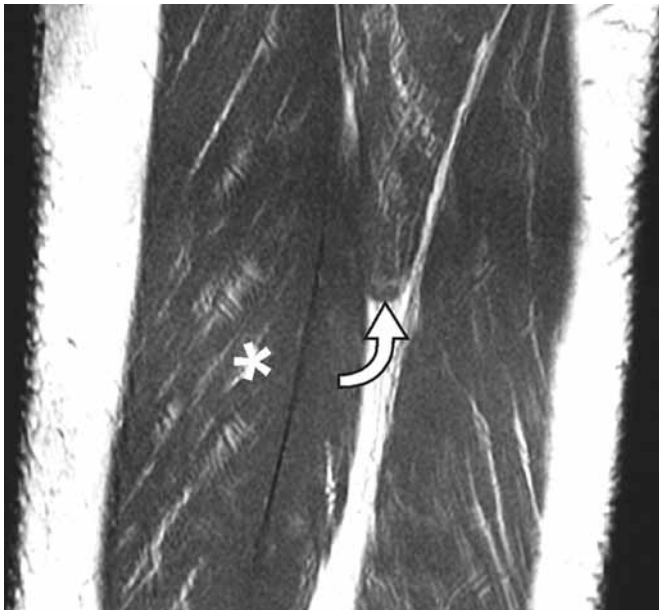


Fig 4: Coronal MR image shows avulsion of the semitendinosus tendon (arrow), with retraction of the muscle. The long head of the biceps femoris muscle is located laterally (*), with the semimembranosus muscle on the medial side.

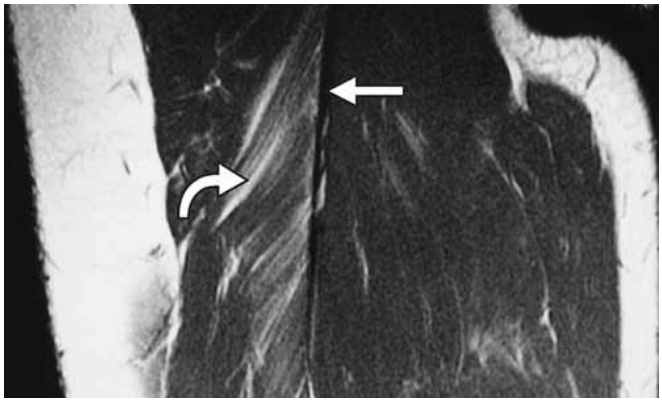


Fig 5: Coronal oblique MR image shows a small region of hyperintensity in the biceps femoris (curved arrow), a finding that is consistent with oedema as a result of a subtle MTJ tear (straight arrow).

The most serious form of HMI is the proximal avulsion. This usually involves the common insertion and in adults does not involve bone (Fig. 2). In adolescents however, the apophysis is weaker than the musculo-tendonous structure and avulsion usually includes the bone. This type of injury is best assessed with MRI as the extent of the tear and tendon retraction are better visualised than ultrasound. In adolescents, the bony fragment is well seen on conventional X-rays (Fig. 3). Proximal avulsions of the hamstring muscles require immediate surgical repair. Distal avulsions of the individual hamstring muscle insertions may occur with ski and football injuries, but are much less common, with semitendinosus insertion avulsions (Fig. 4)

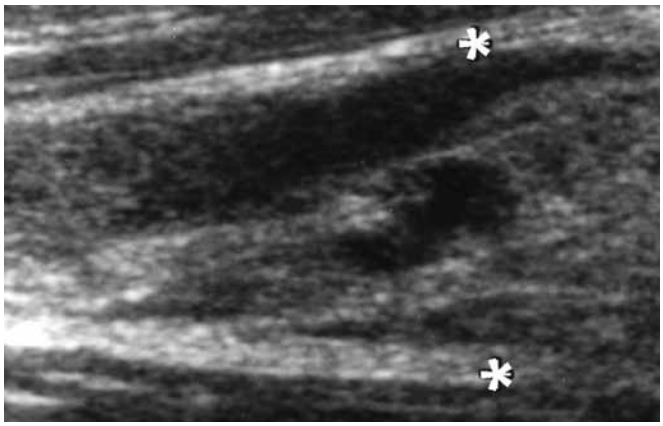


Fig 6: Longitudinal ultrasound image demonstrates a focal area of retraction (*) and hypoechogenicity consistent with a macroscopic tear in the distal MTJ of the semitendinosus.

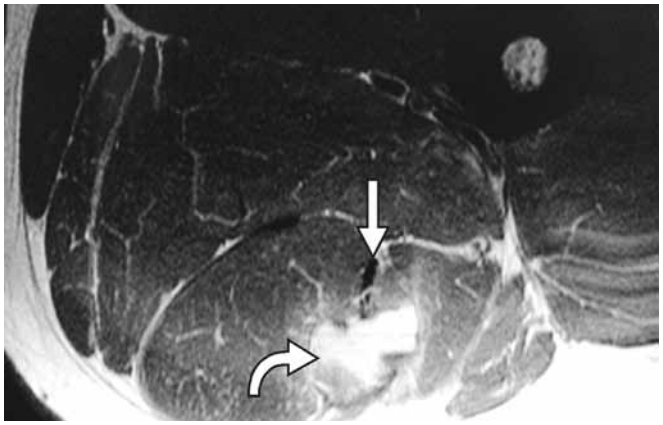


Fig 7: Epimysial fascial strain seen on axial MR image as an area of hyperintensity in the biceps femoris muscle (curved arrow). There is relatively little involvement near the tendon (straight arrow).

being the most common. There is frequently evidence of prior damage to these distal tendons before the occurrence of a tear.

Partial hamstring tears (also known as strains) occur at the MTJ, and more commonly in the proximal MTJ particularly in the biceps femoris muscle. In this case, fluid and blood components lie between the intact myofibrils as they insert into the tendon of the muscle producing a feathered appearance of high signal on MRI (Fig. 5) and as a hypoechoic area on ultrasound (Fig. 6).

Tears may also occur at the junction between the muscle and its surrounding fascia. These are commonly known as epimysial fascial tears (Fig. 7). In contrast, intrasubstance tears present as blood and fluid collections within the muscle that show varying degrees of hyper- or hypointensity depending on the amount and state of the blood components present (Fig. 8). These tears are sometimes referred to as muscle belly tears. Scar tissue is seen on both MR and ultrasound imaging and may contribute to a re-tear of the hamstring muscles due to muscle shortening and diminished elasticity (Fig. 9).

There is a clear correlation between imaging findings and clinical outcome. Tear size is directly related to the number of days lost from competitive sport. Tears exceeding 50% of cross-sectional area of the muscle are associated with prolonged recovery period and most individuals will sustain a re-tear within 2 years. The degree of pain noted is also related to the size of the tear seen on MR imaging or ultrasound and is consequently also related to the length of recovery period. Individuals with clinical suggestion of a tear but no imaging findings show the best recovery rates. If there is imaging evidence of a muscle tear/strain in an athlete in whom this was not clinically suspected, it is advisable to suggest convalescence as continuing the sporting activity would likely lead to progression of the tear and a prolonged recovery period. In the early stages of injury, ultrasound and MR imaging have similar accuracy for lesion detection. In later stages (≥ 2weeks), when the extent of oedema has diminished, MR imaging is more accurate. Deep lesions (more common in muscular athletes) are better assessed with MR imaging. Epimysial injuries, which are more likely to be superficial, are better seen with ultrasound, while MTJ injuries that are generally more deeply located are better seen with MRI.

The importance of imaging findings when planning management of hamstring injuries cannot be understated. With increasing demands placed on athletes and increasing physical activity of the population in general, accurate advice on the management of HMIs is required and this can only be provided with accurate imaging.

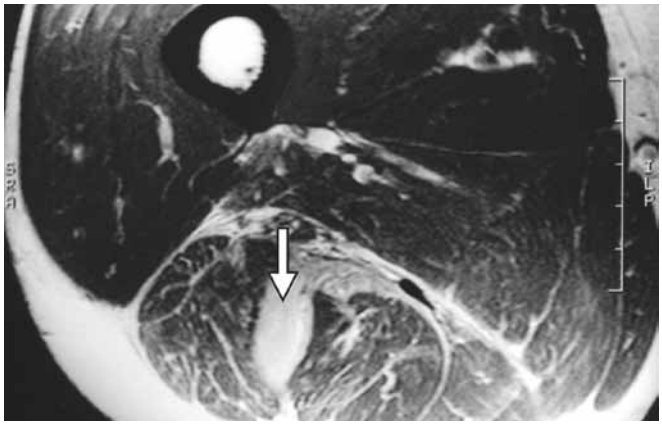


Fig 8: Muscle belly injury seen on axial proton-density–weighted MR image as an intramuscular hematoma in the biceps femoris muscle (arrow).

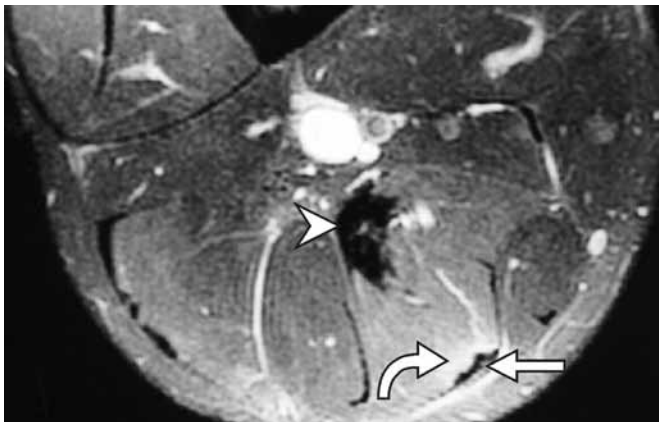
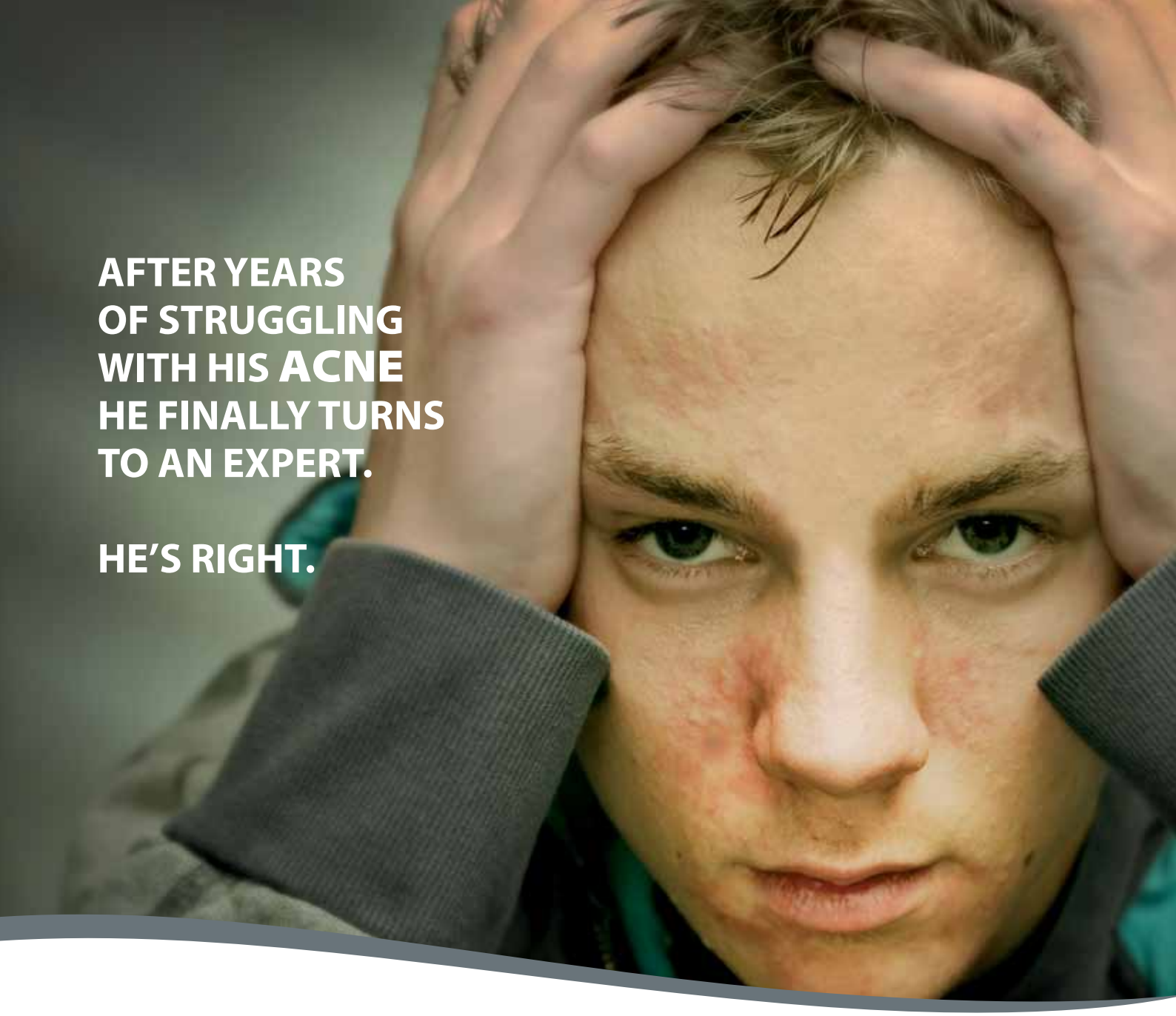


Fig 9: A re-torn semitendinosus muscle. MR image shows an area of hyperintensity (curved arrow) near the semitendinosus tendon (straight arrow) that is consistent with an MTJ tear. However, an irregular area of low signal intensity deep within the muscle (arrowhead) is characteristic of scar tissue following a prior myofascial tear. This may have contributed to the decrease in muscle elasticity ultimately leading to fresh tear.



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References: 1 Terpstra IJ, Acne treatment with 4% erythromycin and 1.2% zinc acetate Cardiff 1988; 255-259. **2** Stainforth J et al. Dermatol Treat 1993 4: 119-122. **3** Schachner L et al. J Am Acad Dermatol 1990; 22(3): 489-495.

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