CEYLON COLLEGE OF PHYSICIANS

MEDICINE UPDATE

2019

Vol :30 No : 01

A Superb Control Works Wonders...

ARBI®

Irbesartan USP 150mg/300mg

Get BP Under Control

- Greater BP reduction than Losartan
- Excellent BP goal attainment
- Provides reno-protective effects
- Lowest cardiovascular events compared to Valsartan, Losartan & Candesartan

PharmEvo®
Our dream, a healthier society

1.1 Should patients with knee osteoarthritis (OA) and comorbidities be encouraged to have exercise therapy?.

126 patients with knee OA and at least 1 comorbid condition such as coronary artery disease, heart failure, Type 2DM, chronic obstructive pulmonary disease or obesity with a BMI exceeding 30 -were randomized to a tailored exercise programme or to standard medical care for 20 weeks. The exercise programme consisted of two 30 – 60 minute sessions weekly with strength training and aerobic exercise. They were also encouraged to exercise at home at least 5 times weekly. At the end of 3 months, physical function scores and 6 minute walk distances improved significantly more in the exercised patients than in the standard care patients.

Comment: Even patients with knee OA and comorbidities benefit from a tailored exercise programme over 3 months. This makes it even more important that clinicians encourage patients with OA of the knees to take regular exercise, muscle strengthening exercises and even upper body exercises.

Ref: de Rooij M. et al Arthritis Care Res. 2017 June; 69: 807

1.2 Is there a place for long term Macrolide (Azithromycin) therapy for uncontrolled Asthma?.

Macrolide antibiotics have antibacterial, antiviral and anti inflammatory effects and thus there is a general interest of using them to treat patients with resistant asthma (not responsive to inhaled corticosteroids and long acting bronchodilators).

420 adults median age 60 with uncontrolled asthma, with inhaled steroids and long acting bronchodilators were randomized to Azithromycin 500mg or placebo **thrice weekly for 48 weeks.** Significantly fewer moderate or severe exacerbations was seen in the Azithromycin group vs placebo (1.07 vs 1.86 per person year). Fewer attacks were seen for both eosinophilic and neutrophilic asthma. Diarrhoea was more common with Azithro and there was a non significant increase in Azithromycin resistant bacteria.

Comment: Long term Azithromycin should be reserved for patients at higher risk for exacerbations and restricted to the cold and rainy moths of the year. Since severe allergic and eosinophilic asthma have specific treatments such as Omalizumab and IL5 monoclonal antibodies, Azithro may be especially attractive for neutrophilic asthma (neutrophils in the sputum and not eosinophils). Biologics may be reserved for resistant cases.

Ref: Gibson P.G. et al Lancet 2017 July 4; e pub

Brusselle G. and Pavord I IBID: e pub.

1.3 Do Bisphosphonates (BPs) prevent hip fractures in chronic Glucocorticoid users?.

BPs are recommended for prevention of osteoporotic fractures. What about chronic Glucocorticoid users?. 1,802 Prednisolone users **over the age of 65** at a dose of >5mg/d for at least 3 months were studied. BPs were started shortly after beginning steroid therapy. They were compared with the same number of patients, of the same age group, who took Prednisolone but no drugs for prevention of osteoporosis. Most of the patients had polymyalgia rheumatica or rheumatoid arthritis. Median prednisolone dose was 8mg daily. During an average follow up of 1.3 years, hip fracture occurred in 10 BP patients vs 27 in non BP patients per 1,000 patient years. Thus, for every 60 steroid treated patients on Alendronate – roughly 1 fewer hip fracture occurred.

Comment: The BP Alendronate which was used in this study can prevent hip fractures in older patients who take daily corticosteroids. Whether these results apply to the average community dwelling out patients is not clear. The American College of Rheumatology recommends BP therapy depending on the patient's age, steroid dose, steroid duration and presence of osteoporosis risk factors.

Ref: Axelsson K.F et al JAMA 2017 July 11; 318: 146.

1.4 Ultrasound guided injections (USGI) vs blind injections (BI) for Carpal Tunnel Syndrome (CTS).

CTS is normally treated with splinting, local steroid injections or surgery. BIs are usually palpation guided using anatomical land marks. A retrospective cohort study was undertaken in 234 patients who had BI and compared with 87 patients who used USGI. The two groups were matched for age, sex, comorbidities etc.

During a mean follow up of 6 years, the likelihood of repeat injection or surgical relief was significantly lower in the USGI group (Hazard ratio 0.59).

44% of USGI patients and 64 % in the BI group required eventual surgery. Most retreatment occurred within the 1st year of follow up.

Comment: This study suggests that outcomes are better with USGI in patients with CTS. In cases of secondary CTS due to hypothyroidism, rheumatoid arthritis, acromegaly and pregnancy - these results may not be the same, but injections may certainly buy time till the primary condition is adequately treated.

Ref: Evers S. et al Arthritis Care Res.2017 July; 69: 1060.

1.5 A new indication for the use of Oxytocin – Autism Spectrum Disorder (ASD).

Oxytocin is a hormone known to cause uterine contractions during labour and in expressing preformed milk during lactation. A new property of Oxytocin is that it improves social behaviour. Autism is a condition in childhood associated with decreased social associations and increased repetitive behaviours. Some of these patients have low levels of Oxytocin while others have normal levels.

In a randomized double blind trial of 32 children (age range 6 – 12 years) with ASD, Oxytocin **intranasally** daily or placebo were compared when given over 4 weeks. When results were analysed without reference to pre treatment Oxytocin levels, the benefit in social behaviour fell just short of statistical significance ($P = 0.06$). However, in children with the lowest pre treatment Oxytocin levels, the improvement in social behaviour was superior to placebo and statistically significant ($P = 0.02$). Children whose social behaviour improved with placebo, also showed increase in endogenous levels of Oxytocin.

Comment: This study shows that daily **intranasal** Oxytocin for 4 weeks improves social behaviour in children with ASD, whose baseline endogenous blood Oxytocin levels are low. The placebo response in ASD might involve a surge in endogenous production of Oxytocin. Interestingly, although Oxytocin treatment improved social functioning, **it did not** affect repetitive behaviours that are also seen in ASD patients. Measurements of serum Oxytocin before a trial of intranasal Oxytocin is necessary.

Ref: Parker K.J et al Proc.Natl.Acad.Sci.USA 2017 July 25; 114: 8119.

1.6 Undiagnosed atrial fibrillation (AF) after cryptogenic ischaemic stroke (CIS).

Long term monitoring of heart rhythm is required for diagnosis of AF, because a substantial percentage of patients with CIS do not exhibit AF, soon after the onset of CIS.

When 256 older patients (age >65), 50% of whom had prior strokes or systemic embolism, and were implanted with subcutaneous ECG monitors, over a mean follow up of 16 months, 90 patients (34%) had at least one episode of AF lasting more than 5 minutes. The following risk factors were noted for the incidence of AF.

1. Left atrial enlargement on echocardiography.
2. Elevated levels of N terminal pro BNP.
3. Lower systolic BP.

Ref: Healey J.S et al Circulation 2017 Aug 4; e pub.

1.7 Do Beta blockers (BB) have a place in the treatment of osteoarthritis (OA)?.

Adrenergic neurotransmission is involved in pain pathways. Recently, several animal and human studies have suggested that BBs have antinociceptive effects. The association between BB use and pain was analysed in a cohort of 873 patients with hip or knee OA and hypertension. 40% of these patients were taking BBs. It was found that BB users were significantly less likely than non users to have at least moderate joint pain (34% vs 42%). After adjustment for various demographic and clinical characteristic, it was found that at least moderate joint pain remained significantly less likely among BB users (OR 0.68). BB users were also less likely to be taking opioid analgesics. No other antihypertensive class of drugs was associated with attenuated pain.

Comment: BBs have recently been dropped to 2nd tier therapy for hypertension except when there is concomitant coronary artery disease. The study above has an interesting finding of a possible analgesic effect of BBs. This could become a relative indication for earlier BB use in patients with both hypertension and OA.

Ref: Valdes A.M. et al Arthritis Care Res.2017 July; 69: 1076.

1.8 Are oral corticosteroids indicated for non asthmatic patients with probable viral bronchitis?.

Acute lower respiratory tract infections (LRTIs) excluding pneumonia, are usually viral in origin and labelled as "viral bronchitis" especially if there is wheezing. These patients often receive oral steroids, because their symptoms are like those seen in asthma exacerbations.

401 adults (mean age 47, 17% smokers) with acute cough + at least one of the following – sputum production, chest pain, wheezing or shortness of breath were enrolled in this study. They were randomized to oral Prednisolone 40mg/d for 5 days or placebo and were then followed up for a further 8 weeks. No significant differences were found between the groups in duration of moderately bad or worse cough (5 days), symptom severity or peak flow.

Comment: These results clearly advice against using oral steroids for treating non asthmatic patients with uncomplicated acute LRTIs. This study does not address whether steroids would benefit patients without previously diagnosed asthma who present with acute bronchitis and marked expiratory wheezing on auscultation.

Ref: Hay A.D et al JAMA 2017 Aug 22; 318: 721.

1.9 A new Vasopressor – Angiotensin II.

The body's natural response to shock is to release Catecholamines and Vasopressin and to activate the Renin – Angiotensin – Aldosterone system (RAAS). The standard care of patients with vasodilatory shock includes infusions of Norepinephrine and Vasopressin. However we have no pharmacologic agents that support the RAAS. Could synthetic human angiotensin II complement the standard Vasopressors in treating patients with shock?.

In a multinational trial, 321 patients with vasodilatory shock (80% with sepsis) were randomized to receive either synthetic Angiotensin II or placebo. All patients were receiving Vasopressors and maintaining a mean arterial pressure (MAP) of 66 mmHg before enrolment. Patients with low cardiac output were excluded. The MAP of 75mmHg or increase in MAP by 10mmHg within 3 hours of infusion initiation was seen in 70% of those on Angiotensin II vs 23% on placebo. Similarly mean increase in MAP was significantly different in the 2 groups – 12.5mmHg for Angiotensin II vs 2.9mmHg for placebo. Mortality was 46% for the Angiotensin II group and 54% for the placebo group (P = 0.12). Adverse events including tachyarrhythmias and distal Ischaemia occurred with equal frequency in both groups.

Comment: Patients with sepsis often have depressed cardiac function and the safety of this medication in that setting was not tested. Convincing evidence of a mortality benefit in vasodilatory shock with the use of Angiotensin II is needed before it can become part of standard clinical practice.

Ref: Khanna A. et al NEJ Med 2017 Aug3; 377: 419.

1.10 Can we predict Bacteraemia in patients with fever who require blood cultures?.

In a study of 1,943 patients with fever admitted to 3 hospitals in Japan, blood cultures were taken. The presence of "shaking chills" and food consumption in relationship to positive blood cultures was analysed. The overall incidence of positive blood cultures was only 11%. The risk for positive blood cultures and the above two features were noted.

a) Shaking chills + poor food consumption - 48% culture positive.

b) Poor food consumptions only - 13% blood culture positive.

c) Normal food consumption but with shaking chills - 4%

d) Normal food consumption and no shaking chills - 2%.

Comment: Combination of shaking chills and poor food consumption is a powerful predictor of positive blood cultures. Empirical antibiotics may be started in these patients after the blood samples are taken for culture.

Ref: Komatsu T et al J.Hosp.Med.2017 July ; 12: 510.

1.11 What is the relationship between serum Triglyceride (TG) levels and the risk for acute pancreatitis (AP)?.

High TG levels is the underlying aetiology in about 2.5% of patients with AP. The commoner causes are gall stone disease and excessive alcohol intake. The mechanism in high TG associated pancreatitis is due to the fact that the excess TG is hydrolysed by pancreatic lipase to give rise to excess free fatty acids (FFAs). The excess FFAs consequently overwhelm the binding capacity of albumin and cause acinar and pancreatic capillary injury. In addition, hyperviscosity resulting from Chylomicromaemia causes impaired pancreatic blood flow leading to ischaema. TG levels between 1,000 – 1,999 mg/dl is classified as "severe" and levels above 2,000mg/dl as "very severe".

In a study of 1,157 adults with serum TG levels above 1,000 mg/dl – the following facts were determined in relation to attacks of AP.

1) The prevalence of AP in this cohort was 9.2%.

2) AP was commoner in those who were young.

3) TG levels above 2,000 mg/dl had greater risk for AP than those below 2,000mg/dl.

4) Presence of gall stone disease and alcoholism further increased the risk.

5) Presence of TG without risk factors in (4) above had less risk.

6) Diabetic ketoacidosis was commoner in those with TG above 2,000mg/dl.

Comment: All patients with acute pancreatitis should have an estimation of the serum TG level. Patients with high TG having undiagnosed abdominal pain, nausea, vomiting and abdominal distension should be investigated to exclude AP.

Ref: Amblee A. et al Endocrine Practice 2018 May; 24(5): 429 – 436.

1.12 Should patients on long term glucocorticoids (GC) with suppressed cortisol levels have glucocorticoid replacement before, during or after surgery?.

GC administration at a systemic dose of **5mg or more per day** of Prednisolone or equivalent, for **longer than 4 weeks** can lead to the development of adrenal insufficiency (AI). This can be detected by an estimation of fasting plasma cortisol below 5 mcg/dl. Should these patients have perioperative GC therapy, as very often fasting plasma cortisols are not done before surgery. Further, should they have supra physiological doses to prevent adrenal crisis because of the risk of increased stress during surgery. Supra physiological perioperative

doses will increase the risk for hyperglycaemia, hypokalaemia and neurocognitive activation. The following facts are pertinent in a study of 188 patients who had GC induced adrenal insufficiency.

1. Adrenal crisis occurred in <1% of the patients considered to be at risk.
2. In patients undergoing surgery without GC replacement, the plasma cortisol levels were found to peak at 4 – 6 hours post surgery and returned to base line after 24 hours. when the surgery was mild or moderately severe.
3. When the surgery was major, the elevated plasma cortisol levels were sustained up to 72 hours.
4. Continuing the usual GC dose without increase or decrease was sufficient to withstand the physiological stress of the surgical procedure and to prevent acute adrenal insufficiency during the perioperative period.
5. Additional GCs perioperatively was found to be unnecessary.
6. Oral GC therapy should not be stopped abruptly before surgery or in the perioperative period.
7. Acute adrenal insufficiency should be looked out for in patients undergoing major surgery and is likely to occur in the first 24 hours of minor surgery and within 72 hours after major surgery.

Ref: *Rushworth* R.L. et al Endocrine Practice 2018 May;24(5): 437 – 445.

1.13 A new Diabetic entity – Very elderly (>85 yrs) new onset diabetes.

With the increase of life expectancy, more people are now living beyond 85 years. Some of these people develop diabetes after 85 yrs. This type of diabetes has the following features.

1. Lean type, low BMI diabetes.
2. Elevated serum amylase compared to those with middle age onset diabetes.
3. Pancreatic weight is decreased.
4. Pancreatic duct obstruction is increased.
5. Pancreatic acini are atrophied.
6. Fibrosis in the pancreas was increased.
7. The islet cell mass was decreased and had increased amyloid.
8. Retinopathy is less common than in middle age onset DM.
9. More prone to hypoglycaemia.
10. Alpha cell mass was increased.

Ref: Xin A. et al JCEM 2017 Sept; 102: 3162 – 3167.

1.14 Glucagon mini dose for non severe hypoglycaemia.

Adults with hypoglycaemia can treat themselves with glucose if they are conscious. If they are unconscious, they will not be able to take oral glucose themselves and the swallowing reflex if not intact, will prevent even a bystander to administer the oral glucose required. In such cases, iv glucose will correct the abnormality and return consciousness. However this requires a competent person to give it intravenously. A convenient alternative is Glucagon which can be administered **subcutaneously** or **intramuscularly**. The **adult dose is 1mg** but has to be reconstituted by a competent person. **In children**, a new Glucagon which is administered sc in a **dose of 150mcg** has now been introduced "DASI GLUCAGON". The preparation is already constituted and available in a device. Therefore it can be administered readily, without delay, by any competent person without requiring intravenous access. It is stable over many years. The blood sugar increases after 30 minutes

and peaks at about 2 hours. The hyperglycaemic effect of Glucagon only lasts up to the next meal. This is different from the effect of oral glucose which may lead to hyperglycaemia, well beyond the next meal.

Comment: Mini dose Glucagon is a convenient method when the patient or bystander cannot administer oral glucose. It avoids unnecessary caloric intake which may last more than the required duration. There may be discomfort at the injection site and nausea. Packaging in a patient friendly reusable device is an advantage.

Ref: Haymond M.W et al JCEM Aug 2017; 102: 2994 – 3001.

1.15 Are Proton Pump Inhibitors (PPIs) safe in Type 2 diabetics?.

The Freemantle Diabetes Study undertook to answer this question in Type 2 diabetes patients on stable ACE inhibitors or ARBs. They were divided into 4 groups.

Group1 No PPIs. (N =686)

Group 2 PPIs throughout the study. (N= 174)

Group 3 Commencing PPIs. (N= 109)

Group 4 Discontinuing regular PPI therapy. (N=67).

Duration of observation was 2 years.

Main outcomes

1. Urine albumin creatinine ratio.
2. eGFR.
3. 5 year CVD risk.

Results:

1. Urine albumin creatinine ratio not affected by PPIs.
2. eGFR was lowest in group 3.
3. CVD risk was greatest in group 3.

Comment: Commencing PPIs in Type 2 DM patients resulted in lowering of eGFR and increase in 5 year cardiovascular disease risk.

Ref: Davis T.M.E et al JCEM Aug 2017; 102: 2985 – 2993.

1.16 Can Alpha blockers be withdrawn in patients with Benign Hypertrophy of the Prostate (BHP) who have been on combination Alpha blockers (ABs) + 5 Alpha reductase inhibitors (ARIs)?.

BHP patients may receive ABs (Tamsulosin, Silodosin) which relaxes prostatic and bladder neck smooth muscle tone and improve urinary flow within a short period, in combination with 5 ARIs (Finasteride, Dutasteride) which reduce prostate size over several months. Can patients receiving both drugs eventually drop the AB without experiencing symptom relapse?.

140 men with BHP >30ml in volume by Ultra sound scan began treatment with both Silodosin and Dutasteride. At 12 months, symptoms scores, prostatic volume and urine flow rates had improved considerably. The group was then randomized to continue combination therapy or to continue Dutasteride only and stop the Silodosin. During a follow up of further 12 months, mean improvements in symptoms scores and urodynamic measurements were maintained with no significant differences between groups.

Comment: This study suggests that after 12 months of combination therapy in BHP, withdrawal of the AB will not exacerbate symptoms. If symptoms worsen, ABs can always be restarted. These findings may not

be appropriate for very large prostates. A rational way of determining whether ABs can be withdrawn is to perform the urine flow rate test. If the maximum flow rate exceeds 15ml/sec, a trial of AB withdrawal may be appropriate.

Ref: Matsukawa Y. et al J.Urol. 2017 Oct; 198: 905.

1.17 Will patients with chronic kidney disease (CKD) benefit from intensive BP lowering therapy?.

Intensive BP control lowers risk for adverse CV events and all cause mortality in high risk hypertensive non diabetic patients. However, its value in patients with CKD (eGFR <60ml/mt) is unclear. A meta analysis of 18 randomized trials in which more intensive BP control (Systolic BP 132 vs 140mmHg) was undertaken with 16,000 patients with CKD. The Base line, Systolic BP was 148mmHg. During a median follow up of 3.6 years, death occurred in 7.8% patients vs 8.4% patients in the intensive and less intensive groups respectively. This indicated a 16% risk benefit which was not statistically significant but indicated a non significant trend for greater mortality benefit.

Comment: Lowering the systolic BP from 148mmHg to 132 mmHg produced a non significant improvement in mortality benefit. The number needed to treat for 1 patient to benefit was 166 (NNT 166). Perhaps even more intensive BP lowering to achieve a systolic BP target of < 120mmHg and continued for a longer period may be more beneficial.

Ref: Malhotra R. et al JAMA Intern Med. 2017 Oct 1st; 177: 1498.

Kovesdy C.P. IBID : 1506.

1.18 For evidence of coronary artery disease – which is better – CT angiography (CTA) or Treadmill testing (TMT)?.

CTA can detect anatomic coronary disease, whereas TMT provides functional evidence of ischaemia. TMT may not be appropriate for patients with unstable angina. A meta analysis from 13 trials in more than 10,000 patients with **stable or acute** chest pain was conducted.

During a mean follow up of 18 months, **all cause mortality** and **cardiac hospitalizations** were similar in the CTA and TMT groups. However, **myocardial infarction (MI)** was significantly less in the CTA patients. (Relative risk = 0.71). However, CTA was associated with significantly higher rates of **invasive coronary angiograms** (12% vs 9%) **Revascularizations** (7% vs 4%) and medical therapy with Aspirin or statins (20% vs 8%).

Comment: In this meta analysis, TMT and CTA performed similarly for mortality and hospitalizations, although CTA was associated **with lower MI rates,** perhaps due to greater use of medical therapy.

Editorialists note that UK guidelines have given CTA a prominent role in evaluating patients with recent onset chest pain. CTA would be more appropriate for patients with dyspnoea and limb deformities which prevent adequate TMTs. TMTs are cheaper and may be the preferred investigation when cost is an important factor.

Ref: Foy A.J. et al JAMA Intern Med 2017 Oct 2nd ; e pub.

Villines T.C. and Shaw L.J. IBID : e pub.

1.19 Treating apathy in Alzheimer disease (AD) – Methylphenidate (MP).

AD patients are treated for memory loss with Donepezil, Memantine or Rivastigmine. These are Choline esterase inhibitors. While they are on this treatment, patients may also be apathetic. These patients may be offered antidepressants. Inspite of this combination, apathy may remain a prominent feature, which impairs motivation, limits spontaneous behaviour and is associated with heavier care giver burning. 60 such patients (mean age 77) who had mild AD were offered MP **10mg b.i.d** or placebo. Many of these patients had hypertension, coronary artery disease and depression. The trial duration was for 12 weeks. The following improvements were noted.

1. Overall apathy at 4 weeks.
2. Behaviour, cognition and motivation by 8 weeks.
3. Depression and emotion scores by 12 weeks.

Adverse events were similar in the two groups.

Comment:

1) Apathy and depression may be separate and treating apathy might help reduce depressive symptoms.

2) Even older patients with hypertension and CVD did not have more adverse effects when used in this modest dose of 10mg b.i.d when compared to placebo.

3) Improvement in all aspects was seen by 12 weeks which is comparable to the time required for improvement with Choline esterase inhibitors.

Methyl phenidate is usually used in children with attention deficit hyperactive disorder. The dose is 5mg b.i.d and increased weekly to a maximum of 30 mg b.i.d.

Ref: Padala P.R et al Am.J.Psychiatry 2017 Sept 15; e pub.

1.20 Cardiac MRI (CMRI) is useful to assess prognosis in myocarditis.

Patients with myocarditis may present with chest pain, tachycardia, arrhythmias, heart failure or be recognized for the 1st time by ECGs and ECHO studies. What about **late Gadolinium enhancement (LGE) in cardiac MRIs ?.** Two studies were undertaken in patients with myocarditis and preserved LV ejection fraction.

In the 1st, an Italian study 384 patients had CMRIs. This showed predominantly inferior lateral wall abnormalities in 41%, anteroseptal in 36% and 16 % in other segments. 7% had no abnormalities. During a median follow up of 4.3 years, anteroseptal late Gadolinium enhancement was associated with worse prognosis and the best independent predictor of death, heart failure, cardiac arrest and defibrillation.

In the 2nd study, 670 US patients with myocarditis had CMRIs performed. Those with late Gadolinium enhancement were more than twice as likely to experience adverse events compared to patients without LGE. Septal, midwall and patchy LGE was associated with almost 3 fold higher relative risk for adverse events.

Comment: Late Gadolinium enhancement seen on CMRIs was associated strongly with adverse events and poor outcomes. Cardiac MRI looking for LGE is a useful investigation in patients with myocarditis.

Ref: Aquaro G.D. et al J.Am.Coll.Cardiol 2017 Oct 17; 70: 1977.

Compiled by: - *Dr Henry N. Rajaratnam*

MD, FCCP, FRCP (Lond.), (Hon) FRACP, (Hon) FSLCGP, FACE, Hon FSLCE

WHICH WOULD YOU PREFER

X-PLENDED®

Rosuvastatin 5mg,10mg & 20mg Tablets

The Super Statin

- Moderate-dose statin therapy is suggested for patients younger than 40 or older than 70 who have CVD risk factors
- Rosuvastatin produced significantly better reductions in total cholesterol and triglycerides, compared with atorvastatin
- Rosuvastatin 20 mg reduced LDL cholesterol significantly more than atorvastatin 20 and 40 mg

PharmEvo®

Our dream, a healthier society

RESTORING
The Essence of Life

Inosita®

SITAGLIPTIN 25mg, 50mg & 100mg

For Balanced Glycemic Control

- Unique Glucose Dependent Dual Mode of Action
- Recommended by AACE Guidelines 2017 as monotherapy or combination therapy
- Initial combination of Sitagliptin with Metformin provide substantial & additive glycemic improvement
- Safest DPP-4 inhibitor for Type 2 Diabetes management
- Attenuates progression of Carotid Intima Thickening in Insulin treated patients

PharmEvo®
Our dream, a healthier society