The recent Faculty of Consulting Physicians of South Africa (FCPSA) congress held in Cape Town was attended by more than 200 delegates, including registrars in internal medicine from South African universities and a significant representation of clinicians from Namibia and Botswana.

The FCP focuses on providing ongoing medical education to support the high standards of specialist care in South Africa. It represents the interests of private practice in association with other stakeholders and engages in all aspects of private specialist care, such as representations to the South African government-led Health Market Inquiry, the evolving concept of a national health insurance (NHI) for South Africa and ongoing support of evidence-based medicine in specialist practice.

South African and international experts presented updates on a variety of topics. This report covers some of these, focusing in each case only on clinical take-home messages.

**Today, the golden age of pulmonology**

**KEY MESSAGES**

**Tuberculosis (TB)**

- TB diagnosis is not complete without an assessment of the level of drug resistance, as South Africa has between 20 000 and 40 000 patients with multidrug-resistant (resistance to rifampicin and isoniazid) disease; about 3% of all TB cases.¹

- Complicated cases of TB such as extreme drug-resistant TB (XDR-TB) or patients experiencing severe, adverse side-effects of standard TB treatment such as hearing loss, should be treated in consultation with a TB expert/pulmonologist or infection specialist, particularly as there are new agents such as bedaquiline available for therapy (currently only in the public sector). Another new TB agent, delamanid, a nitroimidazole, not yet registered by the South African MCC, is available for compassionate use. These new agents, the first new TB agents in some 40 years, can greatly improve outcomes.

- In South Africa, only 11% of patients with XDR-TB have favourable outcomes at five years post-treatment. Overall, treatment outcomes are poor, irrespective of HIV status.²
TB diagnosis
Using the nucleic acid amplification test, Xpert MTB/RIF, a South African study showed that up to one in seven Xpert-positive cases of patients who’d had prior TB were ‘false positives’ because DNA tends to remain present in non-viable, non-intact bacilli still present in a prior TB patient.³ “This is perhaps an over-estimation; it is more likely to be in the order of 5%,” Professor Dheda noted. “Clinicians need to be aware of this possibility.” Bench-top assays of this gene amplification test will soon be available in South Africa.

A point-of-care, urine-based lipoarabinomannan (LAM) test is useful for inpatients, particularly very ill, HIV-infected patients who are not capable of producing a sputum sample. This rapid test applied in a South African situation resulted in a 20% reduction in mortality, because TB was diagnosed in patients in whom traditional testing methods using sputum are very difficult.⁴

Chronic obstructive pulmonary disease (COPD)
By 2030, COPD will be the third most common cause of death globally. The mainstream of pharmacological treatment for high-risk patients is inhaled corticosteroid therapy; the remaining COPD patients should receive treatment targeting symptom alleviation.

Once-daily long-acting beta-agonist/long-acting muscarinic antagonist (LABA/LAMA) combinations plus an inhaled corticosteroid (ICS) or a LABA/ICS are effective with a rapid onset of action, and result in a significant reduction in exacerbations. A number of these agents will soon be available in South Africa.

Asthma
Asthma is a common disease in South Africa with some three million people suffering from it. Five percent have severe asthma, which is difficult to manage. These patients consume 80% of the clinical resources available for asthma therapy. Severe asthma is defined as uncontrolled asthma with exacerbations, despite the patient’s being on a high dose of inhaled corticosteroids plus a second controller agent.

It is vital to check patient adherence and inhaler technique as these are frequently implicated in non-response to treatment. Tiotropium has been shown in a meta-analysis to improve lung function in inadequately controlled asthmatics.³ Bronchial thermoplasty, offered at UCT Private Academic Hospital, is well tolerated and useful in very compromised asthmatics.

New developments in the treatment of HIV/AIDS

**KEY MESSAGES**
- As antiretroviral therapy (ART) is expanded to all HIV-infected persons, regardless of CD4 count, the issue of keeping people in care and virologically suppressed is vital to the long-term prospects of the individual and the community at risk.
- The new policy of test-and-treat in HIV infection, regardless of CD4 count, is evidence-based.

Currently, three million of the 6.4 million HIV-infected South Africans are on ART, of whom 75% remain in care after 12 months; 80% are virologically suppressed. This is just short of the new WHO target, which aims to have 90% of known HIV patients on therapy with 90% maintaining viral suppression over time.

The most vulnerable group at HIV risk in South Africa is that of adolescent girls (15-19 years), in whom the HIV prevalence is 5.6%, compared to boys in the same age group whose prevalence is less than 1%. Urgent action to protect this vulnerable group is essential.

The current South African policy is
still defined by CD4 count. If the CD4 count is below 350 cells/µL, ART is recommended; if between 350 and 500 cells/µL, ART can be started if the patient is motivated; if above 500 cells/µL, ART is not commenced unless there are AIDS-defining illnesses.

Three trials have challenged this approach and have shown clear health advantages to starting therapy early, before CD4 counts fall to below the arbitrary 500 cells/µL. This implies a new ‘test-and-treat’ policy for HIV infection (Table 1). In Europe, the patient’s view is taken into consideration and an individual assessment is made as to the person’s readiness to start ART therapy (Table 2).

Of the three trials, the most pertinent to South Africa is the TEMPRANO trial conducted in the Ivory Coast, where early initiation of ART and six months of isoniazid preventative therapy resulted in a 44% reduction in severe HIV-related illness and a 35% reduction in all-cause death (deferred treatment levels did change during the study). This clinical benefit was also seen in the START trial, which showed a striking 96% reduction in the risk of HIV-1 transmission to sexual partners of persons receiving early ART therapy.

A new antiretroviral, dolutegravir, is now available in South Africa. It has fewer side-effects and a higher barrier to the development of resistance. It may become a new first-line therapy in South Africa.

Pre-exposure prophylaxis for HIV should be given to all who identify themselves as being at high risk. In the South African context, young girls should also be considered for this intervention.

### Table 1. Recommendation 1: When to start ART among people living with HIV

<table>
<thead>
<tr>
<th>Target population</th>
<th>Specific recommendation</th>
<th>Strength of the recommendation</th>
<th>Quality of the evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults (&gt; 19 years)</td>
<td>ART should be initiated in all adults living with HIV at any CD4 cell count</td>
<td>Strong</td>
<td>Moderate</td>
</tr>
<tr>
<td></td>
<td>As a priority, ART should be initiated in all adults with severe or advanced HIV clinical disease (WHO clinical stage 3 or 4) and individuals with CD4 count ≤ 350 cells/mm³</td>
<td>Strong</td>
<td>Moderate</td>
</tr>
<tr>
<td>Pregnant and breastfeeding women</td>
<td>ART should be initiated in all pregnant and breastfeeding women living with HIV at any CD4 cell count and continued lifelong</td>
<td>Strong</td>
<td>Moderate</td>
</tr>
<tr>
<td>Adolescents (10–19 years old)</td>
<td>ART should be initiated in all adolescents living with HIV at any CD4 cell count</td>
<td>Conditional</td>
<td>Low</td>
</tr>
<tr>
<td></td>
<td>As a priority, ART should be initiated in all adolescents with severe or advanced HIV clinical disease (WHO clinical stage 3 or 4) and individuals with CD4 count ≤ 350 cells/mm³</td>
<td>Strong</td>
<td>Moderate</td>
</tr>
</tbody>
</table>

### Table 2. EACS Guidelines 2015: Recommendations for initiation of ART

<table>
<thead>
<tr>
<th>Symptomatic HIV disease (CDC B or C conditions, incl. tuberculosis)</th>
<th>Asymptomatic HIV infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any CD4 count</td>
<td>Correct CD4 count</td>
</tr>
<tr>
<td>&lt; 350</td>
<td>≥ 350</td>
</tr>
<tr>
<td>SR</td>
<td>SR</td>
</tr>
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<td></td>
<td>R</td>
</tr>
</tbody>
</table>
Chronic heart failure

The challenge for the physician treating heart failure is the chronic nature of this disease; in order to treat it effectively there needs to be a partnership between the physician and patient. Importantly, the five-year survival after heart failure diagnosis is similar to that of the major cancers in the developed world, between 26% and 52%.

The most recent ESC Guidelines, released on 21 May 2016, have introduced a new category of heart failure (HFmrEF), which covers patients with ejection fractions (EFs) of 35-50%. These patients fall between the reduced and preserved heart failure categories. In South Africa, symptomatic patients with an EF of less than 50% should be treated within the HFrEF category, according to current South African guidelines.

“It is vital to remember that remodeling occurs in patients after myocardial infarction (MI), the most common aetiology of chronic heart failure, and that subsequent contractile injury results from, among others, myocyte hypertrophy and increased interstitial collagen formation,” Dr Klug pointed out. The systolic functional decline leads to activation of three major neurohormonal systems (Fig.1). Neprilysin inhibitors offer a new therapeutic strategy over and above β-blockers and renin angiotensin aldosterone system (RAAS) inhibitors (ACE-inhibitors, ARBs and spironolactone). The resulting enhancement of the natriuretic peptide system by neprilysin inhibition is a beneficial counter-regulatory system in heart failure. It is important to note that neprilysin inhibition also increases angiotensin II, so new agents in this class must address this issue or be used in combination with RAAS inhibition.

LCZ 696 (sacubitril/valsartan) is a first-in-class inhibitor of both neprilysin and angiotensin II. This combination has been assessed in chronic heart failure patients with reduced EF (LVEF≤35%) and shown to be superior to enalapril in reducing mortality and morbidity in the largest ever trial involving heart failure patients.

As a result of this trial, the most recent ESC Guidelines propose (a class 1, level B recommendation) the replacement of ACE inhibition with neprilysin inhibition in HFrEF patients who remain symptomatic despite optimal treatment with an ACE inhibitor, a beta-blocker and a mineralocorticoid receptor antagonist (MRA) to further reduce the risk of heart failure hospitalisation and death.
Treatment of non-alcoholic fatty liver disease (NAFLD)

**KEY MESSAGES**

- NAFLD is a continuous spectrum of disorders; patients can regress from NAFL or progress to NAFL with mild inflammation, to NASH, to NASH with fibrosis, and to cirrhosis.
- Patients with cirrhosis are at increased risk of death and hepatocellular carcinoma and high-risk symptomatic patients should be screened.
- Obesity is the major cause of the increase in prevalence of NAFLD worldwide, (although the condition does occur in lean people).
- NAFLD is an independent risk factor for features of the metabolic syndrome and cardiovascular events.
- The main clinical aim is to prevent progression of NAFL to fibrosis of the liver and further liver damage.
- Intensive lifestyle modification/weight loss is a proven therapy.
- While there are no drugs registered specifically for the treatment of NAFLD, drugs which can be used, in the absence of contraindications are:
  - Pioglitazone for type 2 diabetic patients
  - Liraglutide for diabetic patients who cannot take pioglitazone
  - Vitamin E for non-diabetes patients without cirrhosis
  - Pentoxyfilline for non-diabetic patients who cannot take vitamin E.

Easier and safer insulin usage with new-generation insulins

The initiation and optimisation of insulin therapy is set to get easier with the introduction of IDegAsp, a co-formulation of insulin degludec and insulin aspart, to South African clinical practice. Professor Roger Chen pointed out that delay in insulin initiation leads to inadequate glucose control and increased morbidity and mortality among type 2 diabetic patients. “The WHO, in its recent global review of diabetes, reported that 43% of all deaths from diabetes in South Africa, an upper middle-income country, occur before the age of 60 years.11 This premature mortality can be improved through better management of type 2 diabetes,” he said.

IDegAsp contains 70% insulin degludec, an ultra-long-acting insulin with a flat time-action profile at steady state, and 30% insulin aspart, a well-known and effective prandial insulin. The two insulins act independently as they are released separately from the subcutaneous depot. “Insulin degludec has been available for some time in Europe and Australia; if used as a basal insulin, it is given once daily, as it has a half-life of 25 hours, twice as long as insulin glargine. It has a flat time-action profile and patients experience less day-to-day variability on this insulin.12 This is a unique benefit of these new-generation long-acting insulins for both type 1 and type 2 diabetes patients,” Dr Chen said. Importantly, insulin degludec at steady state after three days of dosing shows a much lower day-to-day variability compared to insulin glargine.13

The co-formulation of insulin degludec and insulin aspart in IDegAsp co-exists in solution; they remain separated and no resuspension is required. “This means that the distinct basal profile of insulin degludec is combined with the well-known post-prandial action of insulin aspart,” Dr Chen noted.

The effectiveness of insulin degludec as an ultra-long-duration insulin has also been shown in a preplanned meta-analysis of data from seven phase 3 clinical trials (five in people with type 2 diabetes...
and two in people with type 1 diabetes\textsuperscript{14}. It controlled HbA1c to target with a significantly reduced risk of overall and nocturnal hypoglycaemia.

The clinical trial programme included two phase 3a open-label trials of twice-daily IDegAsp dosing versus biphasic insulin aspart (BIAsp 30, at breakfast and their main meal) in people previously treated with insulin. Analysis of these data showed that IDegAsp provided a similar improvement in glycaemic control with a lower risk of hypoglycaemia, particularly nocturnal hypoglycaemia, in these type 2 diabetics.\textsuperscript{15}

In conclusion, Professor Chen stressed that IDegAsp offers flexibility in the timing of administration, along with a unique analogue co-formulation with preserved component action. Patients require less insulin to achieve target glucose levels than with the traditional analogue basal bolus regimen.

References