

Enzalutamide prolongs prostate cancer survival

Adding enzalutamide to standard treatment significantly increases overall survival in men with metastatic hormone-sensitive prostate cancer, showed results from an international study (abstract LBA2).

The study randomized 1125 patients to standard testosterone-suppressing treatment with goserelin, leuprolide or degarelix plus enzalutamide (160 mg once daily) or one of three standard non-steroidal anti-androgens: bicalutamide, nilutamide or flutamide. Nearly half (503) also received early doses of docetaxel. Patients were followed up for a median of 34 months.

Interim analysis at 3 years showed that 80% of patients treated with enzalutamide plus testosterone suppression (with or without docetaxel) were alive compared to 72% of those treated with another non-steroidal anti-androgen. Serious adverse events occurred in 42% of patients taking enzalutamide vs 34% of those on other non-steroidal anti-androgens.

Of 529 men with a low volume of disease on imaging 90% were alive at 3 years vs 82% on other non-steroidal anti-androgens. Increased survival with enzalutamide was particularly marked in men not treated with docetaxel; 83% vs 70% were alive at 3 years.

Immunotherapy improves 5-year survival in patients with advanced non-small cell lung cancer

Treatment of patients with advanced non-small cell lung cancer with pembrolizumab significantly increases overall survival at 5 years, according to results from the longest study yet to be carried out with immunotherapy in this type of cancer (abstract LBA9015).

The KEYNOTE-001 trial included 550 patients with advanced non-small cell lung cancer. Of these, 101 had not previously received any systemic treatment for their lung cancer, while 449 had received prior drug treatment. All patients were treated with pembrolizumab 2 mg/kg every 3 weeks or 10 mg/kg every 2 or 3 weeks for up to 2 years. Pembrolizumab binds to the programmed cell death-1 receptor, potentiating anti-tumour responses by the immune system.

After a median of just over 5 years (60.6 months) 18% of study participants (100 patients) were still alive. Nearly one in four (23%) of those who had not received prior treatment were alive and 15.5% of those previously treated. Five-year survival rates were highest in patients whose tumours had >50% expression of programmed cell death-1 ligand.

‘The uniformly negative outlook previously



Dr Riyaz Shah,
Consultant Medical
Oncologist, Maidstone
and Tunbridge Wells
NHS Trust, Kent

associated with a diagnosis of advanced non-small cell lung cancer is no longer appropriate,’ said lead author Dr Edward Garon, Associate Professor of Medicine at UCLA, Los Angeles, USA. He added, ‘These data confirm the potential of pembrolizumab to improve long-term outcomes for both treatment-naïve and previously treated patients with advanced non-small cell lung cancer.’

‘This study was a key take home for treating advanced non-small

cell lung cancer. We are going from a 5-year survival of around 5% with chemotherapy to 23% with immunotherapy,’ commented Dr Riyaz Shah, consultant medical oncologist at Maidstone and Tunbridge Wells NHS Trust, UK. He said: ‘I have patients who are upset at stopping immunotherapy after the licensed period of 2 years when they are doing well. But we can reassure them that three-quarters of the patients treated for 2 years in this study were still alive at 5 years.’

Considering the tolerability, he noted, ‘There was no new toxicity at 5 years compared to what we are familiar with in our use of these drugs over the last few years.’

Lower dose chemotherapy effective in frail and/or elderly patients

A lower dose of chemotherapy achieves comparable survival but with less toxicity than standard doses in the treatment of frail and/or elderly patients with advanced gastro-oesophageal cancer, showed results from the largest study of optimizing drug treatment in these patients (abstract 4006).

The UK study included 514 patients with advanced gastroesophageal cancer aged 51–96 years. They were randomized to three dosage groups: oxaliplatin 130 mg/m² once every 21 days plus

capecitabine 625 mg/m² twice a day given continuously, the second group received 80% of these doses and the third group received 60%.

Overall treatment utility at 9 weeks was highest in the group given the lowest dose of treatment. Just over one-third of these patients (37%) had non-haematological adverse events of grade 3 severity or higher compared more than half (56%) of those in the higher dose groups.

Overall survival was comparable among the three groups, and progression-

free survival was also non-inferior with the lowest dose compared to the highest dose (hazard ratio 1.10, 95% confidence interval 0.90–1.33).

Lead author Dr Peter Hall, consultant medical oncologist at the University of Edinburgh, suggested: ‘Low-dose treatment may be offered to patients who are suitable for chemotherapy but too frail or elderly for a full-dose standard regimen, in the confidence that it can produce superior outcomes without compromising cancer control or survival.’

Susan Mayor

Antibodies against HPV16 can develop up to 40 years before throat cancer is diagnosed

An international study has found that antibodies to human papilloma virus type 16 (HPV16) develop in the body between 6 and 40 years before a clinical diagnosis of throat cancer, and their presence indicates a strongly increased risk of the disease (Kreimer et al, 2019).

The HPV Cancer Cohort Consortium comprises nine population cohorts from Europe, North America and Australia. In total, 743 incident cases of throat cancer and 5814 controls provided at least one pre-diagnostic blood sample, including 111 cases with multiple samples.

The study also found that having HPV16 antibodies increased the risk of throat cancer far more in white people than in black: nearly 100-fold in white people, but 17-fold in black people. Patients with HPV-associated throat cancer tend to respond better to treatment than those whose cancer is not associated with the infection; the researchers say this may partly explain the worse survival rates among black patients.



Dr Mattias Johansson, Cancer Epidemiologist, International Agency for Research on Cancer, Lyon, France

The main causes of throat cancer (or oropharyngeal squamous cell carcinoma) are smoking, alcohol use and infection with HPV16.

Dr Mattias Johansson, a cancer epidemiologist at the International Agency for Research on Cancer in Lyon, France, who led the research, said: 'Future studies will focus on the most appropriate way to follow up individuals who test positive for HPV16 antibodies and whether there is a way to identify pre-malignant lesions, as well as alternative ways of reducing the risk of eventually developing oropharyngeal squamous cell carcinoma. In other words, there is a long way to go before this biomarker can be used in clinical practice. While vaccination against HPV holds promise in preventing HPV-related cancers, we will not see a resulting reduction in throat cancers for several decades.'

Kreimer AR, Ferreiro-Iglesias A, Nygard M et al. Timing of HPV16-E6 antibody seroconversion before OPSCC: findings from the HPV3 consortium. *Ann Oncol.* 2019 Jun 11. pii: mdz138. <https://doi.org/10.1093/annonc/mdz138>

Natural history of prediabetes in older adults

In the Swedish National Study on Aging and Care-Kungsholmen, 2575 diabetes-free participants aged ≥ 60 years were examined at baseline and followed for up to 12 years (Shang et al, 2019). Diabetes was diagnosed via medical examination, antidiabetic drug use, medical records or glycated haemoglobin (HbA_{1c}) $\geq 6.5\%$. Prediabetes was defined as $HbA_{1c} \geq 5.7\%$ and normoglycaemia as $HbA_{1c} < 5.7\%$ in diabetes-free participants. Data were analysed with multinomial logistic regression.

At baseline, 918 (36%) individuals had prediabetes, of which 204 (22%) reverted to normoglycaemia, 119 (13%) developed diabetes and 215 (23%) died during the 12-year follow-up. The rates of reversion, progression and mortality were higher in the first 6-year period than in the second 6-year period of follow up, albeit not statistically

significant. Lower systolic blood pressure, absence of heart disease and weight loss promoted reversion from prediabetes to normoglycaemia, while obesity accelerated its progression to diabetes.

During the 12-year follow up, most older adults with prediabetes remained stable or reverted to normoglycaemia, whereas only one-third developed diabetes or died. Lower systolic blood pressure, no heart disease and weight management may promote reversion to normoglycaemia, suggesting possible strategies for achieving normoglycaemia in older adults with prediabetes.

Shang Y, Marseglia A, Fratiglioni L, Welmer AK, Wang R, Wang HX, Xu W. Natural history of prediabetes in older adults from a population-based longitudinal study. *J Intern Med.* 2019 Jun 4. <https://doi.org/10.1111/joim.12920>

Multiple adverse outcomes following first discharge from inpatient psychiatric care

Discharged psychiatric inpatients are at elevated risk of serious adverse outcomes. A study has examined the risks of these outcomes (Walter et al, 2019).

Data from the Danish Civil Registration System were used to identify individuals who had been discharged from their first inpatient psychiatric episode at 15 years of age or older. Each was matched with 25 controls without a history of psychiatric admission. Survival analysis was used to estimate absolute and relative risks of all-cause mortality, suicide, accidental death, homicide victimisation, homicide perpetration, non-fatal self-harm, violent criminality, and hospitalisation following violence.

The study included 62 922 discharged individuals and 1 573 050 matched comparators. Risks for all eight outcomes were markedly elevated in the discharged cohort. Within 10 years of first discharge, the cumulative incidence of death, self-harm, committing a violent crime, or hospitalisation as a result of interpersonal violence was 32.0% in the discharged cohort.

Absolute risk of at least one adverse outcome was highest in people diagnosed with a psychoactive substance use disorder at first discharge, and lowest in those with a mood disorder. Risks of suicide and non-fatal self-harm were especially high in the first 3 months post-discharge.

The authors concluded that people discharged from inpatient psychiatric care are at higher risk than the rest of the population of a range of serious fatal and non-fatal adverse outcomes.

Walter F, Carr MJ, Mok PLH et al. Multiple adverse outcomes following first discharge from inpatient psychiatric care: a national cohort study. *Lancet Psychiatry.* 2019 Jul;6(7):582-589. [https://doi.org/10.1016/S2215-0366\(19\)30180-4](https://doi.org/10.1016/S2215-0366(19)30180-4)