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## Immunotherapy for lung cancer – A gamechanger!

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## Game Changers

### AN UPDATE IN AORTIC VALVE INTERVENTION AND EARLY DISCHARGE

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Severe aortic stenosis is common and carries significant morbidity and mortality in an ever-growing elderly population.

It is now fifteen years since the advent of Transcatheter Aortic Valve Implantation (TAVI). The first ever case was performed in 2002.<sup>1</sup> Since then data from randomised controlled trials supporting favourable outcomes with TAVI for patients in whom surgical aortic valve replacement is considered high risk have led to its inclusion in the latest International guidelines for management of valvular heart disease<sup>2</sup>.

The TAVI programme at the Royal Victoria Hospital was commenced in 2008. Over 700 cases have been performed to date. All cases are considered at our regional heart team meeting (comprising a minimum of general cardiologist, interventional cardiologist and cardiac surgeons) and implementation of our early discharge pathway in 2013 has already shown locally that in a cohort of carefully selected patients next day and even same day discharge can be safely facilitated<sup>3</sup>. Currently, cases from Belfast are included in ongoing international registry work around the feasibility and safety of early discharge<sup>4</sup>.

The TAVI programme continues to thrive, providing patients evaluated by our heart team with a transcatheter solution with short recovery time, reduced length of stay in hospital and good outcomes.

1. Cribier A et al. Percutaneous transcatheter implantation of an aortic valve prosthesis for calcific aortic stenosis: first human case description. *Circulation*. 2002; **106**: 3006–3008
2. Nishimura RA et al. “2014 AHA/ACC Guideline for the management of patients with valvular heart disease.”, *J Am Coll Cardiol*. 2014; **63**(22): e57-e185.
3. Noad RL et al. Pathway to earlier discharge following TAVI: Assessment of safety and resource utilization. *Catheter Cardiovasc Interv*. 2016; **87**(1):134-42.
4. <https://clinicaltrials.gov/ct2/show/NCT02404467> (Downloaded 05/07/2017).

### SENTINEL BIOPSY IN VULVAL CANCER – ESTABLISHING A REGIONAL SERVICE IN NORTHERN IRELAND

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Sentinel node biopsy has an established role in the management of breast cancer and an evolving role in melanoma management. It now also plays a key part in the management of selected vulval cancers.<sup>1,2</sup>

It was introduced to Northern Ireland in 2015 and to date 20 patients with vulval cancer, ranging from FIGO stage 1b-3c, have received sentinel node localisation, using a peritumoural injection of Technetium-99 radiolabelled nanocolloid. The sentinel nodes were identified using a GE SPECT CT gamma camera system. In theatre, nodes are located using a hand-held detector, localising the most proximal draining node (sentinel) from the tumour. 90% of sentinel node biopsies were negative for disease. The 2 biopsy-positive patients were of a higher FIGO stage, they underwent groin node dissection and remain disease free.

The GROINSS-V study found that 1-5 % of vulval cancers will metastasise to non-sentinel lymph nodes. This was reflected in our regional experience, with one biopsy-negative patient presenting with metastatic disease within 1 year.<sup>3</sup> This should be interpreted in the context of a 10-15% recurrence rate in vulval cancer overall.

Careful patient selection in accordance with local guidelines and patient counselling preoperatively is of utmost importance. Implementation of this technique has led to a dramatic reduction in rates of groin node dissection with its associated morbidity.

1. Covens et al. Sentinel node biopsy in vulvar cancer: Systemic review, meta-analysis and guideline recommendations. *Gynaecologic Oncology*, 2015; **137**(2): 351-61
2. Guidelines for the diagnosis and management of vulval carcinoma, RCOG guidelines, May 2014.
3. Oonk MH et al. Size of sentinel-node metastasis and chances of non-sentinel-node involvement and survival in early stage vulvar cancer: results from GROINSS-V, a multicentre observational study. *Lancet* 2010; **11**(7): 646-52.

### IMMUNOTHERAPY FOR LUNG CANCER – A GAMECHANGER!

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Cancer evades the ability of the immune system by turning on cell surface proteins which turn off immune-surveillance cells such as T-helper cells<sup>1</sup>. Immunotherapy treatments such as the immune checkpoint inhibitors overcome cancer’s ability to switch off the immune response to altered cells. Randomised trials studying immunotherapy have demonstrated a patient benefit across a number of disease sites, in both curative and non-curative settings.

Pembrolizumab, a monoclonal antibody for the PD-1 receptor (B cells and T cells), has been NICE-approved in 2017 for the treatment of metastatic non-small-cell lung cancer (NSCLC) in second-line therapy and is available via the



cancer drugs fund in England for first line therapy. Immune checkpoints such as the PD-1 receptor down-modulate the immune response as described above. The KEYNOTE-010 trial showed that pembrolizumab was better than standard second-line chemotherapy in terms of disease progression and toxicity<sup>2</sup>. The particularly impressive outcome from many such immunotherapy studies is controlled or absent disease 5 years after starting treatment in a substantial cohort of patients.

Adverse effects from immune checkpoint inhibitors are largely related to overstimulation of the immune system and include pneumonitis, hepatitis, endocrinopathy, skin rashes and gastrointestinal toxicity<sup>3</sup>. There is growing evidence that radiotherapy delivered before or with immunotherapy, increases the likelihood a clinical response, and further investigations are under way<sup>1</sup>.

1. Hanna GG, Coyle VM, Prise KM. Immune modulation in advanced radiotherapies: targeting out-of-field effects. *Cancer Lett* 2015;**368**(2):246-51.
2. Herbst RS, Bass P, Kim DW, et al. Pembrolizumab versus docetaxel for previously treated, PD-L1-positive, advanced non-small-cell lung cancer (KEYNOTE-010): a randomised controlled trial. *Lancet Oncol* 2016;**387**:1540-50.
3. Hanna GG, Illidge T. Radiotherapy and immunotherapy combinations in non-small cell lung cancer: a promising future? *Clin Oncol (R Coll Radiol)* 2016;**28**(11):726-31.

