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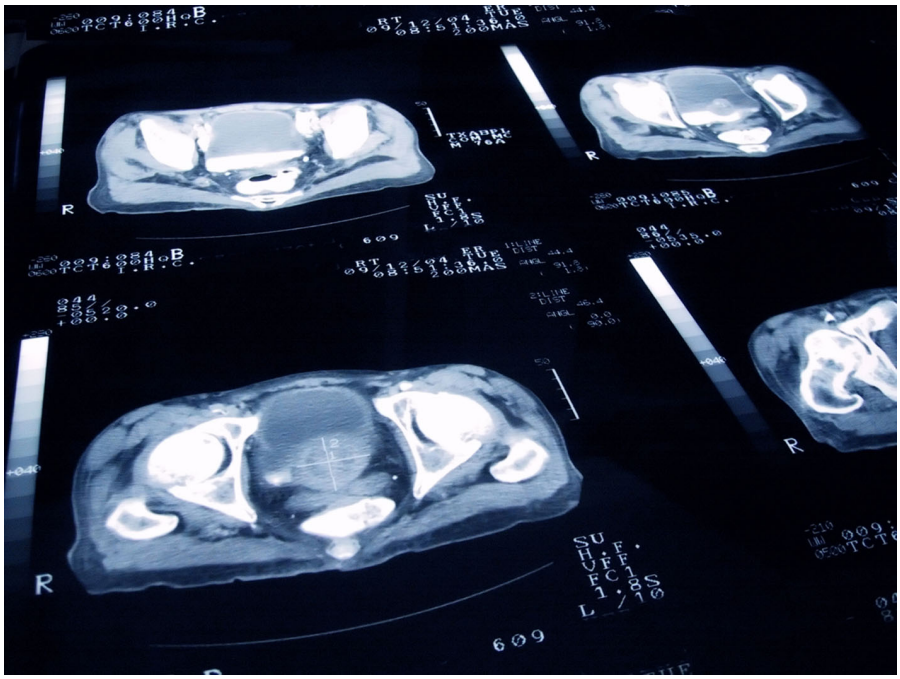
World News

Significant advances in chemotherapy for both urothelial and renal cancer

But are big Pharma more interested in shareholders rather than patients and clinicians?

A purist view of scientific research might suggest that the results of a clinical trial should undergo rigorous peer review before those results are made public. In recent weeks, there have been a number of examples where the results of very significant clinical trials have been the subject of press releases in advance of their presentation at a scientific congress.



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One example is the outcome of the Phase 3 EV-302 trial in patients with untreated advanced urothelial cancer. Astellas Pharma Inc. and Seagen Inc. released the top-line results of this trial on September 22nd 2023, announcing that results from the trial demonstrated superiority for the combination of enfortumab vedotin in combination with pembrolizumab compared with conventional chemotherapy. The results of the clinical trial were actually presented at the European Society of Medical Oncology (ESMO) meeting in October 2023. The trial randomised patients with unresectable locally advanced or metastatic urothelial carcinoma, who had not yet received first-line chemotherapy to receive *either* enfortumab vedotin plus pembrolizumab *or* conventional chemotherapy (gemcitabine plus cisplatin or carboplatin). A total of 886 patients were randomised and the median follow-up was 17.2 months. The study results showed that the new combination resulted in a 55% reduction in the risk of progression compared with chemotherapy (median PFS of 12.5 months versus 6.3 month) and a 53% reduction in the risk of death (median OS of 31.5 months versus 16.1 months). The overall response rate for the new combination treatment was 67.7% and the complete response rate was 29.1%. The most frequent significant adverse events with the novel combination were rash, hyperglycaemia, neutropoenia, peripheral sensory neuropathy, diarrhoea, and anaemia. These results likely represent a step change in the treatment options available for such patients.

https://www.prnewswire.com/news-releases/padcev-enfortumab-vedotin-ejfv-and-keytruda-pembrolizumab-significantly-improve-overall-survival-and-progression-free-survival-in-patients-with-previously-untreated-advanced-bladder-cancer-in-pivotal-phase-3-ev-302-trial-301935662.html
https://www.urotoday.com/conference-highlights/esmo-2023/esmo-2023-press-releases/147438-esmo-2023-keynote-a39-trial-significantly-extends-overall-survival-and-progression-free-survival-in-patients-treated-with-padcev-enfortumab-vedotin-ejfv-and-keytruda-pembrolizumab-in-first-line-advanced-bladder-cancer.html

A second example was the press release by Merck on 1st November 2023, regarding the results of the Keynote-564 trial. This is a randomised, double-blind phase 3 trial for the adjuvant treatment of patients with renal cancer who have undergone nephrectomy and who had either intermediate-high-risk renal cell cancer or high-risk renal cancer or low volume metastatic disease, with complete resection of that metastatic disease. A total of 994 patients had been randomised to receive either pembrolizumab or placebo. The initial results had been published in *NEJM* in 2021 and had demonstrated, with a median follow-up up of just over 24 months, that the disease-free survival was better with pembrolizumab than with placebo. The press release from Merck, reported on the results of one of the secondary end points of the trial, specifically, *"that the drug had met its key secondary endpoint of overall*

survival". The results had been confirmed following a pre-specified interim analysis review conducted by an independent data monitoring committee, and it was noted that the results would be presented at an upcoming medical meeting. At the time of writing that presentation has not yet occurred.

Such pre-presentation press releases by pharmaceutical companies have become commonplace and there are many other examples. One might question whether this reflects a focus upon shareholders rather than clinicians . . . but perhaps that is an old-fashioned view of life.

https://www.nejm.org/doi/full/10.1056/nejmoa2106391
https://www.merck.com/news/keytruda-pembrolizumab-significantly-improved-overall-survival-os-versus-placebo-as-adjuvant-therapy-for-certain-patients-with-renal-cell-carcinoma-rcc-following-nephrectomy/

UK Government announces "Biggest prostate cancer screening trial in decades"

On 19th November 2023 (International Men's Health Day) the new Secretary of State for Health and Social Security in the United Kingdom, the right honourable Victoria Atkins MP announced what was described as *"the biggest prostate cancer screening trial in decades"*. Funding for the research will come from the National Institute for Health and care Research (NIHR) who will provide £16 million and the charity Prostate Cancer UK, who will provide £26 million. The trial is due to start in spring 2024 with recruitment likely to begin in autumn 2024.

https://www.gov.uk/government/news/biggest-prostate-cancer-screening-trial-in-decades-to-start-in-uk

In the same press release, the Secretary of State announced a plan to recruit the UK's first ever Men's Health Ambassador, and to establish the first Men's Health Task and Finish group. The membership of the group would include behavioural scientists, Men's Health campaigners, experts and academics, and they would focus on how to get more men to engage with their health. The UK Government also announced an intention to deliver a host of improvements and updates to those NHS England websites that are most used by men, including those pages relating to issues such as prostatitis, testicular cancer and low sperm count.

> *"In the pilot study, the authors noted the 20% reduction in prostate cancer mortality at 16 years"*

In relation to the screening trial, called TRANSFORM, the press release noted that the trial would use "innovative screening methods like MRI" to detect prostate cancer and it also stated that at least 10% of the screened population would be black men. Beyond that, very little detail was provided within the press release and there was a similar paucity of detail, at the time of writing, on both the NIHR and the Prostate Cancer UK websites. It seems likely that the MRI technology previously reported in *BMJ Oncology* by a team based at University College Hospital London will be the methodology used in the trial. The *BMJ Oncology* trial reported a pilot study, where over 2000 men were invited to attend for a screening MRI and a PSA test. The MRI scan was a clinical and research specific T2 scan without contrast enhancement. A total of 303 men completed both screening tests and 16% had a positive screening MRI, while an additional 5% had a raised PSA density. Following usual assessment for prostate cancer within the British National Health Service, 9.6% of men were diagnosed with clinically significant cancer (although the definition of clinical significance is becoming increasingly problematic and challenging for such trials) and 1% were diagnosed with clinically insignificant cancer. The authors noted that two in three men with a positive screening MRI had a PSA less than 3 ng/mL. One of the other notable aspects of the study was that older white men were most likely to accept the screening invitation, with black men having only a 20% acceptance rate of white men.

In that pilot study, the authors noted the 20% reduction in prostate cancer mortality at 16 years that had been reported within the European Randomised Screening for Prostate Cancer study using PSA. Professor Caroline Moore, the senior author of the study noted *"The UK has a much higher age-standardised prostate cancer mortality compared to countries such as Italy, France, Germany, Spain and the USA. We know that a formal screening approach can reduce prostate cancer mortality, but using PSA and TRUS biopsy alone leads to unacceptable overdiagnosis. The UK has led the world in using MRI to reduce over-diagnosis in men referred for hospital investigation. A new screening study will combine modern diagnostics and trial design with a pro-active formal screening approach, to see if the benefits of modern diagnostics can be used in the screening setting."*

It seems reasonable to assume that the recent UK Government press release reflects a decision to give the green light to a trial that tests this hypothesis.

https://bmjoncology.bmj.com/content/bmjonc/2/1/e000057.full.pdf

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