Evaluate Vantage

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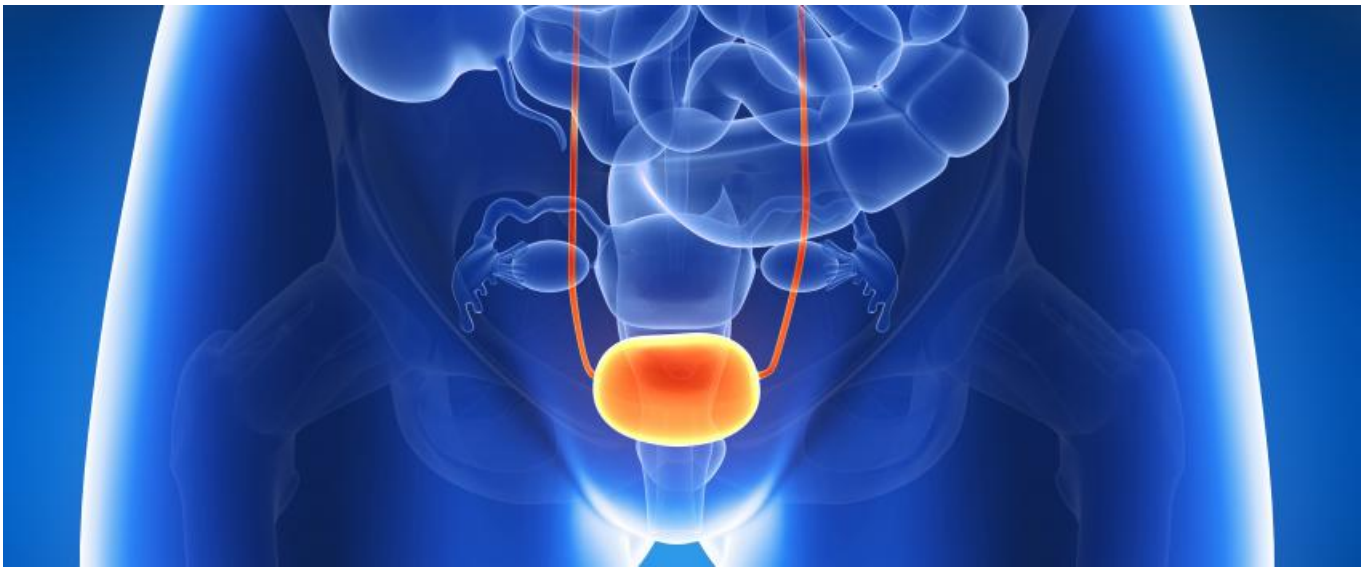
Asco-GU – Bristol in pole position with Opdivo's adjuvant use

Jacob Plieth



Bladder cancer is the fourth tumour type to give Opdivo a phase III adjuvant win, and the extent of the survival benefit is impressive.

The extent of Opdivo's benefit in adjuvant bladder cancer, to be detailed for the first time at its upcoming Asco-GU presentation, underlines strides Bristol Myers Squibb is making in turning around the fortunes of its flatlining PD-1 inhibitor.

The company's push into perioperative uses has now yielded pivotal wins in four tumour types, and success in the Checkmate-274 bladder cancer study comes in contrast to Roche's rival Tecentriq, whose Imvigor-010 trial in the same setting was a bust. With Merck & Co expected to get a grilling today at a US adcom over a separate neoadjuvant/adjuvant use Bristol has it all to play for.

Bristol revealed last September that Checkmate-274 had succeeded in showing Opdivo to extend disease-free survival versus placebo in high-risk, muscle-invasive urothelial carcinoma, but the data were kept back until Asco-GU, where they are to be presented in full this Friday.

High recurrence

In a patient population doctors describe as having high risk of recurring, Opdivo after surgery nearly doubled median disease-free survival to 21.0 months, versus 10.9 months for placebo recipients, amounting to a 30% reduction in disease recurrence at any point in the trial (p=0.0006), the just unveiled abstract reveals.

This was across all-comers, one of Checkmate-274's co-primary metrics. The other, in a cut of those expressing ≥1% PD-L1, was even more positive, the risk reduction amounting here to 47% (p=0.0004). An Asco-GU statement called these benefits clinically meaningful, but cautioned that further follow-up was needed to show any impact on overall survival.

Bristol said it would now discuss the study data with regulators, but it is not clear whether a disease-free survival benefit alone will be enough to secure approval in this cancer type.

Bristol's other three perioperative successes comprise oesophageal cancer in the Checkmate-577 trial, NSCLC in Checkmate-816, and melanoma in Checkmate-238. Like Merck's Keytruda, Opdivo is approved for adjuvant melanoma treatment.

Separately, perioperative treatment of triple-negative breast cancer is under the spotlight because of Merck's

US filing for Keytruda on the basis of the Keynote-522 trial, which is being discussed today by a US FDA advisory panel.

Keynote-522 had a controversial design because it included a neoadjuvant stage, where Keytruda was given before surgery to shrink tumours, as well as an adjuvant one, and it was impossible to discern the specific contribution of each one.

Either way, it looks like Merck will face a grilling, based on briefing documents released this week that revealed more fundamental concerns about Keynote-522. The advice called the clinical benefit demonstrated questionable, and said event-free and overall survival results were “immature and unreliable”.

Summary of pivotal immunotherapy trials in perioperative settings		
Cancer	**Positive**	**Negative**
Melanoma	Opdivo adjuvant use approved (CM-238) Keytruda adjuvant use approved (KN-054)	
Oesophageal	Opdivo adjuvant (CM-577)	
NSCLC	Opdivo neoadjuvant (CM-816)	
Urothelial bladder	Opdivo adjuvant (CM-274)	Tecentriq adjuvant (Imvigor-010)
TNBC	Tecentriq neoadjuvant & adjuvant (Impassion-031) Keytruda neoadjuvant & adjuvant (KN-522)	
Ovarian		Tecentriq 1L & neoadjuvant (Imagyn-050)

For its part, Bristol points out that Checkmate-274 is the first study of an immunotherapy to succeed in adjuvant treatment of high-risk, muscle-invasive urothelial carcinoma.

A year ago Roche said Tecentriq had failed to extend disease-free survival in this tumour, as tested in Imvigor-010, and though it later presented analyses supporting an effect in patients with detectable circulating tumour DNA this trial remains a failure.

The bladder cancer treatment paradigm for immunotherapy is already rather complex. Keytruda and Tecentriq both have front-line labels in certain patients, Merck KGaA/Pfizer’s Bavencio is approved in the maintenance setting, and several other anti-PD-(L)1 MAbs can be used second or third line.

With Opdivo apparently set to add adjuvant use to its approved indications things are unlikely to become any simpler.