Evaluate Vantage

October 02, 2018

Esmo 2018 preview – Another first-line renal cancer showdown

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Once again Europe's premier oncology meeting provides the perfect venue for big pharmas including Pfizer, Roche and Astrazeneca to showcase important pivotal study results, among which another renal cancer battle could be the highlight.

As soon as Bavencio's Javelin Renal 101 trial yielded an unexpectedly strong topline result the question everyone wanted answered was whether an abstract could be submitted for Esmo by the September 17 deadline. Last week investors got their answer as the study appeared in the Esmo late-breakers.

When the meeting gets under way in Munich on October 19 the full results will be scrutinised to ascertain just how big a threat they are for Exelixis – déjà vu for the biotech group, which faced a similar challenge from Bristol-Myers Squibb at Esmo 2017. Beyond that Tecentriq's Impassion-130 readout in breast cancer will get attention, as will numerous combination studies.

For now only the presentation titles have been unveiled by Esmo. Most abstracts will remain under wraps until October 9, oral presentation texts will not be revealed until midday of the meeting's first day, and the embargo on late-breakers will not lift until the start of the session in which each is presented.

This presages an anxious wait for Exelixis investors, who a year ago saw their group's first-line renal cancer results in the Cabosun study overshadowed by late-breaking presentation of data from Bristol-Myers Squibb's Checkmate-214. Now Javelin Renal 101 threatens something similar (*Pincer movement squeezes Exelixis in kidney cancer, September 12, 2018*).

Full data

Javelin Renal 101 is among several pivotal trials whose results have been toplined but whose full data have been kept for Esmo and have been selected for the meeting's plenary session, called the presidential symposium.

Two other such trials are Impassion-130, the most advanced immunotherapy trial in triple-negative breast cancer, which has read out positively for progression-free survival, and Solo-1, which in June made Lynparza the only Parp inhibitor to show a PFS benefit in first-line maintenance treatment of BRCA1/2-mutated ovarian cancer.

Also sure to get its share of attention will be the Keynote-048 study of Keytruda in first-line squamous head

and neck cancer. The Merck & Co drug is already approved second line, as is Bristol's Opdivo, while Astra's Imfinzi had its own first-line study, Kestrel, briefly put on clinical hold.

Selected Esmo 2018 presentations				
Study	**Project**	**Company**	**Abstract**	**Notes**
Javelin Renal 101	Bavencio + Inlyta	Pfizer/Merck KGaA	LBA6_PR	1st-line renal carcinoma, positive for PFS in all comers
Impassion-130	Tecentriq	Roche	LBA1_PR	1st-line triple-negative breast cancer, positive for PFS
Solo-1	Lynparza	Astrazeneca	LBA7_PR	Maintenance ovarian BRCA1/2 mut ovarian cancer, positive for PFS
Keynote-048	Keytruda	Merck & Co	LBA8_PR	1st-line squamous head & neck cancer, positive for OS
Solar-1	Alpelisib	Novartis	LBA3_PR	HR+/Her2- PI3KCA mut breast cancer, positive for PFS
Finesse	Lucitabin	Clovis	289PD	HR+ Her2- metastatic breast cancer; Servier handed back rights Aug 2018
NCT02150967	Infigratinib	Bridgebio Pharma	LBA28	Selective pan-FGFR kinase inhibitor, licensed from Novartis
NCT02825836	M7583	Merck KGaA	1014PD	First-in-human trial, BTK inhibitor in B-cell malignancies
Keynote-200	Cavatak	Merck & Co	LBA40	Oncolytic virus acquired with Viralytics, Keytruda combo
MK-1308-001	MK-1308	Merck & Co	414PD	Externally sourced anti-CTLA-4, combo with Keytruda
Keynote-202	BL-8040	Biolinerx	1133PD	Keytruda combo in metastatic pancreatic adenocarcinoma
NCT02923531	X4P-001-RD	X4/Sanofi	1134PD	Opdivo combo in renal cell carcinoma unresponsive to Opdivo monotherapy
MK-1454-001	MK-1454	Merck & Co	LBA15	First-in-human study of Sting activator, monotherapy or Keytruda combo
NCT02492789	INCSHR1210	Jiangsu Hengrui/Incyte	LBA27	Anti-PD-1 MAb, 2nd-line hepatocellular carcinoma
NCT02627274	RG7461	Roche	412PD	Anti-FAP MAb-IL2 fusion protein, single-agent cohort
NCT02264678	AZD6738	Astrazeneca	413PD	ATR serine/threonine kinase inhibitor, Imfinzi combo
Paloma-3	Ibrance	Pfizer	LBA2_PR	OS data (secondary endpoint), known to be negative

Away from the limelight of presidential symposia Merck will also feature in two presentations of assets it has bought in.

Keynote-200 showcases Keytruda combined with Cavatak, an oncolytic virus it had acquired along with the Australian company Viralytics in February. Oncolytic virus approaches are seeing increasing interest on account of their combination potential, and have generated significant business development activity.

And the "externally sourced, internally refined" anti-CTLA-4 asset MK-1308 will feature in an early trial combining it with Keytruda. Liver cancer data for another asset derived externally, Incyte's anti-PD-1 MAb INCSHR1210, could generate interest, especially now that a sixth PD-(L)1 asset – Sanofi/Regeneron's Libtayo – has secured US approval.

The spotlight will, of course, fall on combinations in general, notwithstanding the blow of this year's failure of Incyte's epacadostat in Echo-301. Keynote-202, for instance, combines Biolinerx's BL-8040 with Keytruda, and is among the industry's most advanced pancreatic cancer studies.

That and several other immuno-oncology studies in patients unresponsive to prior checkpoint blockade could show whether these combos have any potential, and will ensure that Esmo is relevant not only for big pharma followers.