Evaluate Vantage

July 11, 2022

Exelixis unlikely to move Bristol's renal needle for now

Jacob Plieth

Bristol Myers Squibb and Exelixis have shown that adding a small molecule to dual checkpoint blockade can delay disease progression in first-line kidney cancer, but this is unlikely to help them catch up with Merck & Co in this space. Interim analysis of the Cosmic-313 study showed that Cabometyx on top of the approved Opdivo plus Yervoy combo cut risk of progression or death by 27%. So far so good, but Bristol's problem is that Opdivo plus Yervoy itself cuts risk by just 18% versus Sutent, Pfizer's benchmark renal cancer drug against which Merck's Keytruda plus Lenvima scored a stunning 61% reduction in Keynote-581. Thus – on a very rough cross-trial basis – the Cosmic-313 triplet seems to have beaten Sutent by something like 40%, which will not move the needle against Keytruda plus Lenvima. Exelixis fell 5% in early trade today. Overall survival remains an unknown quantity, and while it was not significant in Cosmix-313's interim analysis this could be down to statistical allocation. For now Bristol/Exelixis would do better to stick with the approved Opdivo plus Cabometyx combo, as Yervoy will likely add toxicity – though how much remains unknown until we see the full data.

The first-line renal cancer battleground				
	Keytruda + Lenvima	**Opdivo + Cabometyx**	**Opdivo + Yervoy**	**Opdivo + Yervoy + Cabometyx**
Trial	Clear/Keynote-581	Checkmate-9ER	Checkmate-214*	Cosmic-313*
Comparator	Sutent	Sutent	Sutent	Opdivo + Yervoy
mPFS	23.9mth vs 9.2mth	16.6mth vs 8.3mth	11.6mth vs 8.4mth	Not given
	HR=0.39 (p<0.0001)	HR=0.51 (p<0.0001)	HR=0.82 (not stat sig)	HR=0.73 (p=0.01)**
mOS	NR vs NR	NR vs NR	NR vs 25.9mth	Not given
	0.66 (p=0.0049)	0.60 (p=0.0010)	0.63 (p<0.0001)	Not stat sig at interim

*Note: *in intermediate/poor-prognosis patients; **on a cross-trial basis Opdivo + Yervoy + Cabometyx would be expected to yield an HR for PFS versus Sutent of 0.60 (0.82 times 0.73). Source: product labels and Exelixis press release.*