

AstraZeneca

Price 4,615p

CONDOR and KESTREL: patient recruitment suspended

Fair Value 5220p (+13%)

BUY

Bloomberg	AZN LN
Reuters	AZN.L
12-month High / Low (p)	5,220 / 3,774
Market Cap (GBP)	58,374
Ev (BG Estimates) (GBP)	70,901
Avg. 6m daily volume (000)	2 744
3y EPS CAGR	-3.6%

Observation of higher-than-expected incidence of bleeding in two phase III trials investigating the durva/treme combination in head and neck cancer (1L and 2L) has led to the decision to suspend patient recruitment. Until further assessment of the responsibility of the drugs, it is difficult to act on numbers (ours are reasonable and much lower than CS's), but it will not be easy for any investor to BUY until the topic gets more clarity and better understanding about underlying issues, if any.

ANALYSIS

- At the very end of the trading session yesterday, news came out that patient recruitment has been suspended for two important phase III trials investigating the combination of PD-L1 antibody durvalumab with CTLA-4 inhibitor tremelimumab in head in neck cancer. AstraZeneca has been informed by investigators about a high incidence of bleeding events in the trials and has decided, after discussions with healthcare authorities, to suspend the recruitment until further evaluation (the FDA has suggested a 30-day review).
- The two trials are KESTREL (first-line) and EAGLE (second-line) and unlike HAWK and CONDOR, also in Head and Neck (but two phase II trials), were still recruiting patients. It is not known whether an imbalance across arms has been identified, although it could be assumed that the combination arm durva/treme carries more risk than others. The company is indeed rightfully stressing that the condition of H&N cancer by itself carries a higher risk of bleeding because the cancer is often located close to large blood vessels. However, KESTREL is first-line and started recruiting only one year ago: high incidence of bleeding events is more likely to be drug-related than not, although it is premature to say. Regulators should now take the entire spectrum of studies in H&N to assess the responsibility of any of the treatments investigated either in monotherapy or in combination and decide whether risks outweigh benefits in any of them.
- Although not perceived to be as central to durvalumab's case as lung cancer, H&N is clearly the second biggest indication the drug is looking after. And because Opdivo already delivered strong OS data in 2L, KESTREL is key to potentially open 1L H&N to the durva/treme combination. It is worth noting that both Merck and BMS are investigating their PD-1 compounds in 1L H&N, first in KEYNOTE 048 (pembro alone or pembro+CT) and the second one in CHECKMATE-651 (nivo in combination with ipilimumab, i.e. a very similar design to KESTREL). Could we reasonably think that durva/treme can have a higher haematological toxicity than nivo/ipi? How should we assess the probability of the combination to develop unacceptable haematological toxicity leading to permanent discontinuation of the combination? Would it extend to lung cancer?

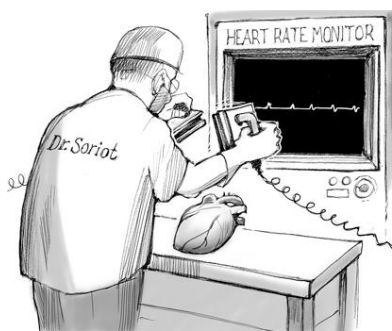
VALUATION

- It is very difficult to say what the implications of the suspension of recruitment for KESTREL and EAGLE ultimately will be for durva/treme in H&N because it could prove balanced across the arms in the end. With USD2.4bn in sales in 2022 for durva and treme combined, we are well below consensus (around USD4bn) and at this stage we do not want to cut this number, considering that H&N is about 20%-25% of the total vs lung cancer.
- That said, an investor cannot ignore the piece of news and raised concern around the durva/treme combination is obviously very bad news for sentiment and will not make easy a BUY call on AZN until uncertainties are lifted. It is likely to play an APHINITY-like type of reaction in most of investors' minds i.e. prevents them from investing short-term because the key take-away message from our recent meeting with Pascal Soriot is that Oncology is key to reach mid-term targets.

NEXT CATALYSTS

- 10 November 2016: Third-quarter results

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