WILSONS ADVISORY

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Theme Alert

Sector Healthcare

Company

Immutep Limited (IMM)

ESMO updates

Dr Melissa Benson
melissa.benson@wilsonsadvisory.com.au
Tel. +61 2 8247 6639

Dr Shane Storey
shane.storey@wilsonsadvisory.com.au
Tel. +61 7 3212 1351

Investment View

We maintain our OVERWEIGHT rating and $1.05/sh risked PT on Immutep. The additional ESMO data, notably the biomarker, and durability of response (DoR) data, continue to support our positive thesis in the differentiated mechanism of Efti and its ability to broaden and enhance the utility of current blockbuster anti-PD-1/L1 agents (such as Keytruda).

Announcement Highlights

Over the weekend additional data has been presented at the European Society for Medical Oncology (ESMO) congress from the TACTI-003 Phase IIb trial of Efti plus pembrolizumab in metastatic head and neck cancers (mHNSCC). Specifically, in an oral presentation further evaluation of the Cohort A data was detailed – the randomized portion of the trial including PD-L1 positive tumours (CPS>1%). We would highlight three new pieces of data since the June topline data: 1) Duration of response (DoR) of 17.5 months for the Efti + Keytruda combo vs 17.1 months for Keytruda alone, remembering that current SOC DoR is ~6 months; 2) one additional partial response (PR) in the Efti combo arm lifting ORR to 34.5% (from 32.8% vs 26.7% in Keytruda control arm); and 3) biomarker data demonstrating clear immune cell recruitment aligned with responders, demonstrating clear support for Efti's mechanism of action. The latter data point is critical in our view, as it quells any prior theories that Efti is not synergistic in its immune recruitment and activation when added to Keytruda, on the basis of the CPS 1-19% subgroup data where comparable ORR were seen. We have seen clarity in the ESMO presentation demonstrating clear imbalances in both of the Cohort A PD-L1 subgroups, which favour the Keytruda control arms. Notably, for CPS 1-19 groups, HPV positive status was materially higher in the Keytruda monotherapy arm (53.8% vs 30.8% in Efti combo arm), with HPV-positive associated HNSCC known to have a better prognostic outlook (as we have detailed previously) and thus likely explaining the astounding Keytruda response in this cohort (~2x all historical trial response rates). The high DoR does give us more confidence in OS data to come, noting that the LEAP-010 trial (Keytruda +LENVIMA) had high PFS and ORR vs SoC but failed on OS (with DoR of 10.1months). In summary, DoR and biomarker data are incremental positives supporting our view that Efti does have a place in the treatment of HNSCC – albeit, we await Overall Survival (OS) data (still to come) to sway our current stance and broaden Efti's commercial opportunity in mHNSCC to all PD-L1 subgroups (not just the CPS <1% cohort we limit to at present).

Wilsons' View

Initial analysis

CPS 1-19% cohort most impacted by HPV-positive status. The ESMO presentation has shown imbalances by CPS subgroup and reaffirms that the HPV-positive imbalance previously called out is materially skewed in CPS 1-19. HPV-positive patients comprised 53.8% in the Keytruda control arm, vs only 30.8% in the Efti + Keytruda arm (1.75-fold diff). This skew was similar in the CPS ≥20 groups albeit far less pronounced (40.7% vs 27.3%). This and the increased number of larynx based primary tumour sites were the two major imbalances in the CPS 1-19 groups, with HPV-positive status a known prognostic indicator in HNSCC response to treatment (i.e. HPV+ better outcomes) which could explain the remarkably high response rate in the monotherapy arm. Unfortunately, this imbalance was not controlled for in stratification at enrolment, noting the logistical challenges we have previously outlined on this point. We take comfort in understanding a clear potential driver of Keytruda outperformance in CPS 1-19 and not that there was Efti + Keytruda underperformance in this subgroup.

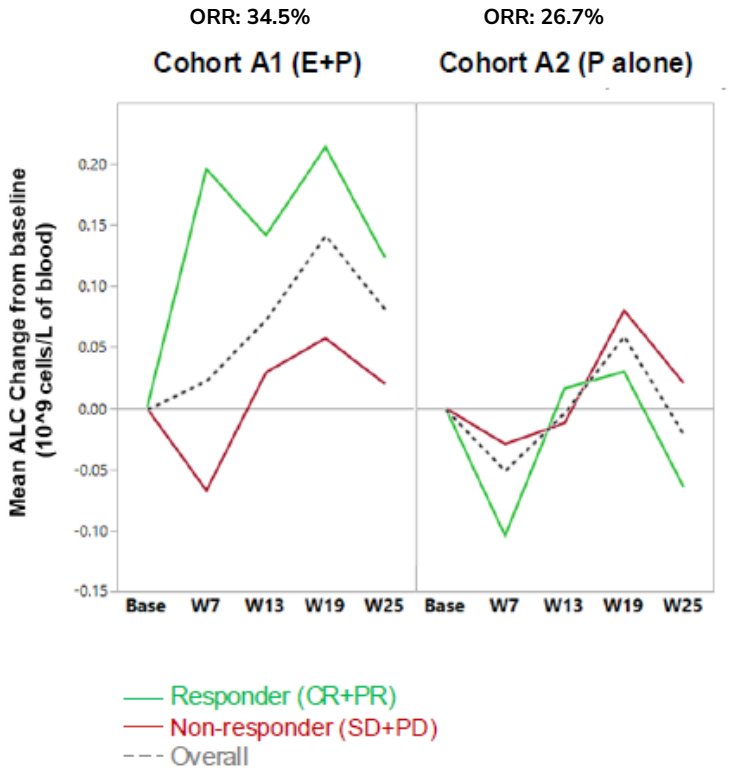
Biomarker data clearly supports Efti's MOA. Whilst this may sound like an obvious statement, there are many drug development programs, including those with approved drug assets where mechanism of action is either a) unknown, or b) not demonstrated with biomarker data during its development. **Figure 1** clearly demonstrates alignment of immune cell recruitment with Efti administration, and further, aligns with responders in this setting – core to the mechanistic thesis of Efti demonstrating on an immune recruitment level there is synergy to its administration in combination with an anti-PD-1.

Bristol Myers updated on their LAG-3 prospect in NSCLC. Separately, BMY have presented data from their Phase II NSCLC program with their anti-LAG-3 drug, relatlimab, combined with their blockbuster anti-PD-1 (nivolumab) and chemotherapy. This triple combination draws some parallels to IMM's upcoming TACTI-004 Phase III triple-combination trial. Median PFS of 9.8 months in PD-L1 TPS ≥1% was reported for the LAG-3 triple combo vs 6.1 months for nivolumab + chemo comparator. This compares to 11.2 months mPFS for Efti + Keytruda (minus chemo) from TACTI-002. BMY are moving this combo into Phase III in metastatic NSCLC (NCT06561386) however are focused only on TPS 1-49% and non-squamous subtypes – a narrower approach vs TACTI-004's all comers design.

Earnings implications

No changes, remembering that we recently removed the PD-L1 positive cohorts (CPS 1-19% and ≥20%) from our HNSCC valuation. Whilst this data update does not drive us to change this conservative view, we are positively bolstered by the biomarker data shown which clearly supports immune recruitment in these patients, and that the DoR bodes well for OS data down the line which could change our stance.

Figure 1: Biomarker data from Cohort A of TACTI-003 demonstrating increased immune cell (lymphocyte count) associated with Efti (E+P) adminstration (stratified by patient response) vs Keytruda alone (P)



Source: Kristensen CA et al. ESMO presentation; 15 Sept 2024.

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Wilsons Advisory contact

For more information please phone: 1300 655 015 or email: publications@wilsonsadvisory.com.au