WILSONS

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Theme Alert

Sector Healthcare

Company

Immutep Limited (IMM)

Final 2L HNSCC data: still doubling ORR

Recommendation OVERWEIGHT

12-mth target price (AUD) $0.91

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Announcement Highlights

Immutep have released two abstracts submitted to the ASCO conference (June 2-6th) in Chicago, which include trial design for their recently initiated AIPAC-003 study in metastatic breast cancer, as well as final data from Part C of the Phase II TACTI-002 trial in 2L head and neck squamous cell carcinoma (HNSCC). The HNSCC final data confirms that the addition of Efti to Keytruda (pembrolizumab) is able to boost response rates, when comparing to standard of care. The key metric (and primary endpoint for TACTI-003)- objective response rate (ORR)- was double that of prior trials of pembrolizumab monotherapy (15-17% on PD-L1 unselected basis, versus Efti's 30% ORR) and importantly was consistent with the last interim readout at ASCO 2021. This ORR impact was even further pronounced in high PD-L1 expressing cohorts (CPS ≥20). Comparisons to prior interim survival (mOS) from mid-21 shows a decline in the overall survival benefit delta (now in line with SOC), albeit is on an all comers basis, with PD-L1 selected data yet to be unveiled (which is the most relevant to IMM's TACTI-003 program). Consistent ORR superiority over SOC cannot be underplayed. We expect further data once posters are released at the conference. In our view today's data continues to support the ability of Efti to expand and increase the addressable market for pembrolizumab in a very difficult to treat patient population. We of course look to TACTI-003 for next clinical data, evaluating this same combination only in 1L patients, with expected topline in 2H CY23.

Wilsons' View

Initial analysis

Figure 1. Cross trial comparisons with pembrolizumab monotherapy in mHNSCC (1L and 2L)

PD-L1 subgroup	Median PFS			ORR			Median OS		
	Efti + pembro (2L)	pembro (2L)	pembro (1L)	Efti + pembro (2L)	pembro (2L)	pembro (1L)	Efti + pembro (2L)	pembro (2L)	pembro (1L)
Trial	TACTI-002	KEYNOTE-040	KEYNOTE-048	TACTI-002	KEYNOTE-040	KEYNOTE-048	TACTI-002	KEYNOTE-040	KEYNOTE-048
All (unselected)	2.1months	2.1months	2.3 months	**30%**	15%	17%	8.7 months	8.4 months	11.6 months
CPS ≥1	NR	2.1months	3.2 months	NR	NR	19%	NR	8.7 months	12.3 months
CPS ≥20	**13.6 months**	NR	3.4 months	**60%**	NR	23%	**15.5 months**	NR	14.9 months

NR: Not reported

Source: IMM, trials as referenced.

Equivalent survival in double the cohort. We of course preface our commentary with the note that this data is from a small (n=37), non-placebo-controlled study, and that comparisons to larger registrational Phase III RCTs are flawed (but necessary) for comparison. Notwithstanding this, the Efti combination has shown largely equivalent progression-free survival (PFS) and overall survival (OS) when comparing to 2L pembrolizumab monotherapy (**Figure 1**), however importantly this has been achieved in approximately twice as many patients (ORR 30% with Efti vs 15-17% pembro only), making a strong case for the ability of Efti to increase the responder rate to pembrolizumab monotherapy. This is further pronounced in the higher PD-L1 cohorts (CPS≥ 20) beating 1L.

OS moderation from ASCO 2021 interim readout. Comparisons to the ASCO 2021 interim readout of mOS 12.6months (now 8.7 months) and ORR of 29.7% (consistent on ITT basis) for the total cohort (PD-L1 unselected) highlight a reduction in total OS benefit delta in the final read presented today. The mOS superiority (~3-4months) over pembro monotherapy the Efti combination previously demonstrated (at interim read) has been lost, however importantly the response rate is consistent (at 29.7%) and still ~2x that of pembrolizumab monotherapy with no additional toxicity. A further important consideration is the duration of response, still not met with minimum follow up at 17 months. This is a key positive perhaps underappreciated by the market.

Current SOC utilises chemo; a durability toss-up. We note that current SOC typically involves use of chemotherapy +/- anti-PD-1 therapy (i.e. pembrolizumab). When comparing the data presented for the Efti + pembrolizumab combo versus KEYNOTE-048 trial data (albeit in a 1L setting; **Figure 2**), ORR of 30% compares well against the chemo combo achieving a response rate (ORR) of 36% - however with the chemotherapy combination having key drawbacks of only a 6.7-month duration of response (with Efti combo duration still not met and tracking >17 months), and a high toxicity profile (Grade ≥3 AEs >70% vs ~10% range for Efti combo based on past reporting).

Figure 2. Comparison of Efti vs other checkpoint inhibitors/chemo in mHNSCC

	Efti + pembrolizumab	Pembrolizumab	Nivolumab	Platinum-based chemo		Pembrolizumab	Pembro+ chemo	Cetuximab + chemo
	IO - IO	IO monotherapy	IO monotherapy	SOC		IO monotherapy	IO - Chemo	SOC
Checkpoint target	PD-1+ LAG-3	PD-1	PD-1	NA	NA	PD-1	PD-1	NA
Study	TACTI-002 Part C	Keynote-040	Checkmate-141	Keynote-040	Checkmate-141	Keynote-048	Keynote-048	Keynote-048
Phase	II	III	III	III	III	III	III	III
Therapy Line	2L	2L	2L	2L	2L	1L	1L	1L
n	37	247	240	248	121	301	281	300
Demographics (% male)	90%	84%	82%	83%	85%	83%	80%	87%
Median age	63	60	59	60	61	62	61	61
PD-L1 TPS <1%	33%	42%	30%	38%	31%	<50% =78%	<50% = 77%	<50% = 78%
PD-L1 TPS ≥1%	62%	58%	37%*	61%	50%*			
PD-L1 CPS ≥1	65%	79%	NR	77%	NR	85%	86%	22%
PD-L1 CPS ≥20	41%	NR	NR	NR	NR	44%	45%	78%
Median PFS	**2.1 months**	2.1months	2.0 months	2.3 months	2.3 months	2.3 months	4.9 months	5.2 months
PF at 6 months	**32%**	25%	20%	22%	10%	25%	45%	45%
Median OS	**8.7 months**	8.4 months	7.5 months	6.9 months	5.1months	11.6 months	13.0 months	10.7 months
Median Duration of response	**>17 months**	18.4 months	NR^	5.0 months	NR^	22.6 months	6.7 months	4.5 months
ORR	**29.7%**	14.6%	13.3%	10.1%	5.8%	16.9%	36.0%	36.0%
Response criteria	iRECIST	RECIST v1.1	RECIST v1.1	RECIST v1.1	RECIST v1.1	RECIST v1.1	RECIST v1.1	RECIST v1.1
Treatment-related Adverse Events (AEs)								
Discontinuation AEs	5%	6%	NR	5%	NR	0%	8%	9%
Grade ≥3 AEs	10%	13%	13%	36%	35%	17%	72%	69%
Leading to death	0%	2%	1%	4%	1%	1%	4%	3%

NR - not reported. ^Qualitatively noted DoR greater in nivo group vs SOC

* Remainder of group of were not quantifiable in their PD-L1 expression levels.

Source: IMM, trials as referenced, Wilsons.

What does this mean for TACTI-003? The first point to note is the challenges with comparison of 1L and 2L cohorts. We do not see a clear readthrough from today's data to the TACTI-003 trial (in 1L HNSCC), in terms of lack of mOS superiority over a pembrolizumab monotherapy comparator. Directionally, the ability to expand response rates (ORR) with the addition of Efti to pembrolizumab aligns with Efti's mechanism, to aid in a fuller immune recruitment to kill tumour cells. We note that the TACTI-003 trial primary endpoint is ORR, with a focus on Cohort A which includes only CPS ≥1 selected tumours. The abstract presented did not provide CPS ≥1 data to compare to the last ASCO 2021 interim read. This data is expected to be included in the poster presentation released following the conference. As a reminder, the last interim read in CPS ≥1 reported ORR of 45.8% and mOS of 12.6 months. Provided ORR is maintained (as it was for the total cohort between interim read and now – at 29.7%) there is clear superiority in responder rates anticipated with Efti addition. On this basis we have more confidence in the ability for TACTI-003 to reach its primary endpoint of ORR superiority over pembrolizumab monotherapy (in CPS ≥1 cohorts). With regards to overall survival benefit – we look to the poster presentation in early June (following ASCO release) for relevant CPS ≥1 data updates. And reiterate our view, that based on this data Efti is providing an important responder benefit when added to anti-PD-1 therapy in a challenging to treat patient population, that have already failed 1L chemotherapy treatment. And that this ability to double pembrolizumab responder rates is strategically attractive to pharma partners.

Earnings implications

None.

Investment view

We maintain our OVERWEIGHT rating and $0.91 per share risked PT.

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