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Investor Update

ASCO 2022 Special Edition

June 2022

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MARC VOIGT

Message from the CEO

As the world's biggest clinical cancer research conference, ASCO is always a very significant event on Immutep's calendar. This year was extra special as we announced new and exciting clinical results from Part A of our Phase II TACTI-002 trial of our lead product candidate, eftilagimod alpha, or efti.

This Part of the trial is evaluating efti when given in combination with our collaboration partner MSD's anti-PD-1 therapy KEYTRUDA® (pembrolizumab) in 114 patients with 1st line non-small cell lung cancer (NSCLC).

Importantly, the trial met its primary objective, delivering promising efficacy in this large indication and warranting late-stage clinical development of efti in this indication.

Key results were:

- The combination of efti plus pembrolizumab shows very good anti-tumour activity, compared with e.g. pembrolizumab monotherapy
- An improved Overall Response Rate (ORR) of 38.6% compared with data last reported
- Encouraging responses observed in all PD-L1 status groups, including those patients with PD-L1 negative and PD-L1 low expressing tumours who are less likely to respond to anti-PD-1 monotherapy
- The combination was safe and well tolerated

The results were presented via an Oral Presentation to thousands of scientists, clinicians, and pharma & biotech executives in a packed auditorium hall at ASCO by TACTI-002 Principal Investigator, Dr Enriqueta Felip of Vall d'Hebron University Hospital Barcelona, Spain. See photo right.

We are also continuing the TACTI-002 trial in the other two indications (2nd line NSCLC and head & neck cancer) and look forward to reporting further data on these parts of the trial in due course.

This special edition of our newsletter provides a detailed outline of the key results presented at ASCO and what comes next.

Above: TACTI-002 Principal Investigator, Dr Enriqueta Felip presents Immutep's trial data at ASCO attracting an audience of thousands of attendees to the presentation.

ASCO 2022 the world's biggest cancer conference

ASCO's annual meeting represents the world's largest gathering of oncology physicians, industry representatives, researchers, patient advocates, and investment analysts to discuss cutting-edge clinical research and therapeutics in oncology, and to gain insights for improving cancer care.

More than 40,000 attendees from around the world join in person and online to stay up to date on new clinical cancer advances in every area of cancer research and gain real-time insights from world-renowned faculty.

For additional information visit www.asco.org.

BASELINE CHARACTERISTICS

The baseline characteristics tell us about the patients as they entered the trial.

TACTI-002 was designed to be unselected for a patient's PD-L1 status to help us understand if efti could help kick start the immune system in patients who were low or negative for PD-L1 and weren't expected to have an optimal benefit.

It is very rare for a trial to be designed without selecting for PD-L1 status. Many trials focus on patients with PD-L1 expression or TPS score of more than 50%.

In TACTI-002, we had patients across the PD-L1 expression spectrum. This makes it an *all-comers* trial.

In fact, more than 70 per cent of patients had a TPS score of less than 50%.

All other patient characteristics reflect what you would typically see in this late stage non-small cell lung cancer patient population, for example the median age was 67 years old and 95% were smokers.

Why is PD-L1 status important and how is it measured?

PD-L1 status is a very important biomarker indicating the likelihood a patient will respond to pembrolizumab.

It is measured with a Tumor Proportion Score (TPS) which is the number of positive tumor cells divided by the total number of viable tumor cells multiplied by 100%.

Patients are categorised as:

- < 1% - called PD-L1 negative
- 1-49% - called PD-L1 low expressors
- ≥ 50% - called PD-L1 high expressors

KEY SAFETY RESULTS

Treatment Emergent Adverse Events (TEAE)	n (%)
Any TEAE	113 (99.1)
Any Serious TEAE	45 (39.5)
Serious TEAE *related to study treatment*	**10 (8.8)**
Any Grade ≥ 3 TEAE	59 (51.8)
***Grade ≥ 3 TEAE related to study* treatment**	**12 (10.5)**
Any Grade 4 TEAE	5 (4.4)
Any Grade 5 TEAE	12 (10.5)
Grade 5 TEAE related to study treatment	**3 (2.6)**
Any TEAEs leading to discontinuation of study treatment	23 (20.2)
TEAEs leading to discontinuation related to study treatment	**11 (9.6)**

Importantly, the combination of efti and pembrolizumab was safe and well tolerated.

Overall, the safety profile is consistent with that observed in previously reported studies for pembrolizumab monotherapy, except for local injection site reactions (erythema). This is due to the mechanism of action of efti, which activates cells locally under the skin when injected.

Some grade four and five treatment emergent adverse events (TEAEs) were observed. However these were not linked to treatment, but to the underlying disease.

Only 11 patients, 9.6%, discontinued their treatment which is normal even for pembrolizumab monotherapy.

KEY EFFICACY RESULTS

38.6%
OVERALL RESPONSE RATE

73.7%
DISEASE CONTROL RATE (DCR)

PRIMARY OBJECTIVE MET

Overall Response Rate

The primary objective of the trial was Overall Response Rate (ORR) as measured according to the iRECIST methodology. To meet our primary objective, this part of the trial had to reach an ORR equal to or higher than 35%.

At ASCO, we reported an ORR of 38.6% in the intent to treat population, which is the most conservative approach and includes all patients who have been recruited to the trial. If you just look at patients who are evaluable for efficacy, meaning they have at least one CT scan, the response rate increases to 42.7%. See table below.

The trial has therefore met its primary objective.

Importantly, if we calculate ORR using an alternative standard methodology, called RECIST 1.1, the ORR is 37.7% making it very consistent with iRECIST.

In addition, we saw comparable response rates in squamous (ORR of 35%) and non-squamous (ORR of 38.9%) tumour types.

Tumour Response[1] (data cut-off 15 April 2022)	**Part A 1st line NSCLC (N=114)**	
ORR as per iRECIST by local read (primary endpoint)	**n (%)**	[95% confidence interval][2]
ORR (ITT, N=114)	44 (38.6%)	[29.6-48.2]
ORR (evaluable patients, N=103)	44 (42.7%)	[33.0-52.9]

ORR by PD-L1 Status

When looking at the ORR breakdown by PD-L1 status, it's important to note the responses we observed were across all PD-L1 groups:

- PD-L1 status of < 1%: ORR 28.1%
- PD-L1 status of 1-49%: ORR 41.7%
- PD-L1 status of ≥ 50%: ORR 52.6%

It is very encouraging to see that even patients who would be less likely to respond to pembrolizumab monotherapy, respond to the combination therapy with efti.

Importantly, the reported ORRs are favourable compared to historical trials of anti-PD-1 monotherapy in all the different PD-L1 status groups.

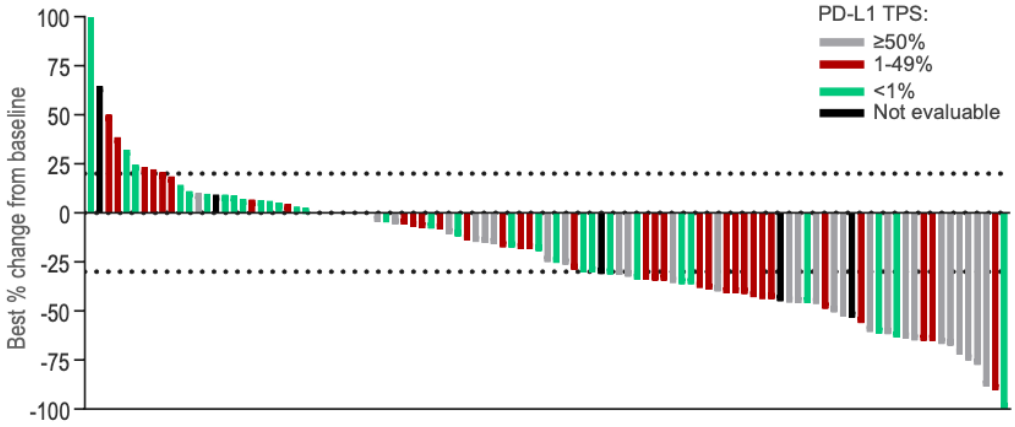
Disease Control Rate (DCR)

Disease control was achieved in 73.7% of patients in the intent to treat population and 81.6% for evaluable patients, meaning that more than 70% of the patients had a clinical benefit. Importantly, disease control was comparable across all PD-L1 status groups with a range of 68.8-79.0%.

[1] Local investigator evaluation.
[2] 95% CIs calculated using Clopper-Pearson test.

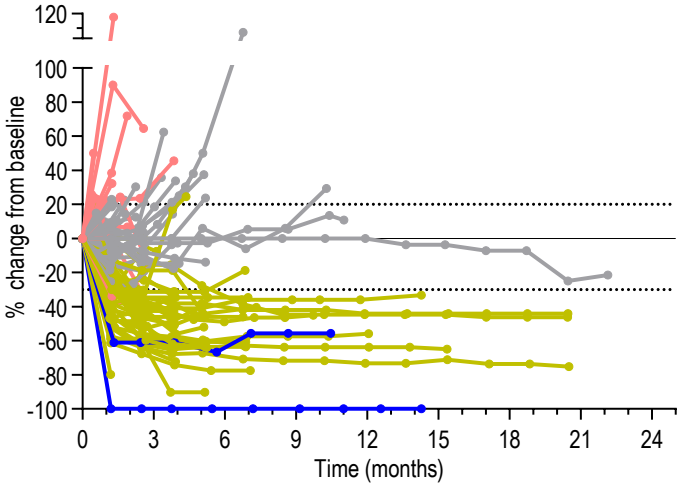
DEPTH & DURABILITY OF RESPONSE

Encouragingly, two patients had a complete response where their target tumours disappeared altogether. Overall, 19.4% of the patients had a decrease of 50% or more in the size of their target tumours, telling us the responses are deep. In addition, there's a significant decrease in the size of the tumours in all the PD-L1 subgroups.



Above: The waterfall plot shows the change in lesion size from baseline for 1st line NSCLC patients from TACTI-002. Each colour represents a different PD-L1 status group (see legend).

After six months, only very few patients had disease progression if they had initially responded to the combination therapy. Only 8.6% of the patients with a confirmed response progressed within the first six months which is comparable with pembrolizumab alone.



Above: The spider plot tracks the patients' journeys over time showing the duration of response or the duration of stabilisation of disease, which is equally important to the depth of the response. The blue lines indicate patients with a complete response, the greenish yellow indicates patients with the partial response, gray indicates patients with stabilisation of disease, and pink indicates patients with progressive disease.

The duration of response is one of the key differentiating factors of combining two immuno-oncology therapies (such as eft and pembrolizumab) compared to an immuno-oncology therapy plus chemotherapy. Importantly, the median duration of response has not yet been reached, which is promising.

COMPARISON TO OTHER THERAPIES

By benchmarking our TACTI-002 results against other approved treatments, the efti and pembrolizumab combination compares favourably.

Looking at historical trials reported for pembrolizumab monotherapy (KN-001 & KN-042 trials), pembrolizumab monotherapy is known to have poor efficacy for patients with a TPS score under 50%, which represents around 70% of patients. This is a large group of patients with unmet medical need.

Double chemo and anti-PD-1 combinations can deliver an increased ORR and overall survival, however they offer a substantially shorter duration of response due to the chemo, which also brings high toxicity for patients.

Immutep therefore sees the efti and pembrolizumab combination fitting into the landscape by extending the use of pembrolizumab for patients with a TPS above 1% and extending the use of chemo and pembrolizumab combinations.

In particular, the efti and pembrolizumab combination could be especially beneficial for PD-L1 low expressors.

TPS	Treatment	Efficacy[1]	Toxicity AEs leading to disc.
0 – 100%	Efti + Pembro	ORR 38.6% PFS 6.9 mts	< 10%
	Doublet Chemo	ORR 19-30% PFS 5-9 mts	8-22%
	Doublet Chemo + Pembro	ORR 48% (NSQ) & 63% (SQ) PFS 6 (SQ) & 9 (NSQ)	14%
	Doublet Chemo + Atezo + Beva	ORR 56% PFS 8.4 mts	33%
	Doublet Chemo + Ipi + Nivo	ORR 38% PFS 6.7 mts	19%
≥ 1%	Efti + Pembro	ORR 45.5% PFS 8.4 mts	< 10%
	Pembro mono	ORR 27.5% PFS 5.4 mts	1-14%
	Ipi + Nivo[2]	ORR 36% PFS 5.1 mts	18%
≥ 50%	Efti + Pembro	ORR 52.6% PFS 11.8 mts	< 10%
	Pembro/Atezo/Libtayo mono	ORR 35-45% PFS 7-10 mts	1-14%

CONCLUSION & WHAT'S NEXT

The combination of efti plus pembrolizumab is showing favourable efficacy in 1st line NSCLC in the PD-L1 all-comer population and in all PD-L1 status groups. We have reported an ORR of 38.6% which is very promising compared to historical control studies. Patient responses are deep and durable and, importantly, the trial has continued efti's good safety profile.

The data reported at ASCO supports the continued late-stage development of efti in this indication. Additionally, due to the positive data from efti presented at ASCO and other conferences, Immutep has been approached for potential new investigator-initiated trials as well as other potential collaborations for efti in various indications and combinations which we are currently assessing. It is very encouraging to see the increased level of industry interest and willingness to support and fund further trials for efti as a result of the growing body of positive data generated from our efti clinical trials thus far.

To read more about our TACTI-002 results, please see:

- A replay of our **Global Webcast** & **Accompanying Presentation**
- ASX announcement of the **ASCO Results**

FOLLOW IMMUTEP'S PROGRESS

Immutep is dedicated to maintaining consistent and clear communications with our investors. In addition to our newsletter, we encourage our shareholders to continue following Immutep's progress in a number of ways:

www.immutep.com

Our website is a treasure trove for those in search of details about our company, our management team, and archived information. We encourage everyone to check it out regularly.

www.clinicaltrials.gov

Immutep registers all of our clinical trials, and the details of enrolling doctors, on the ClinicalTrials.gov website, a service of the United States National Institutes of Health. This register is the largest such repository of clinical trial information around the world.

Our ClinicalTrials.gov ID for our trials are as follows:
- AIPAC trial is NCT02614833
- TACTI-002 trial is NCT03625323
- T ACTI-003 trial is NCT04811027

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This investor update was authorised for release by the CEO of Immutep Limited.