The study is sponsored by Innate Pharma and supported by AstraZeneca.

The study consists of 2 parts: a dose-escalation part and a cohort expansion part. Results from the dose-escalation part of the study are presented here.

Figure 2: Dose-escalation part – 4 dose levels

Table 1: Immunologic effects on MDSC and neutrophils (Figure 1). Our preliminary data suggest that the combined blockade of C5aR and anti-PO (1,1) synergistically reduce tumor growth and delay tumor progression 8.

Furthermore in lung cancer mice models, C5a blockade controls the growth of established and/or metastatic tumors with anti-PO (1,1) 9.

These data suggest that combining IPH416, with an anti-PO (1,1) may improve efficacy and overcome secondary resistances to anti-PO (1,1) therapies.

Main inclusion criteria for the dose-escalation part:

- Patients with advanced and/or metastatic histologically-confirmed hepatocellular carcinoma (HCC), urothelial carcinoma (UCC), renal cell carcinoma (RCC) or NSCLC
- Systemic therapy in the metastatic setting.

Secondary objectives:

- To evaluate the time to progression (TTP) of patients with IPH5401 in combination with durvalumab
- To determine the immunogenicity of IPH5401 administered in combination with durvalumab

Table 2: Best tumoral response by tumor type (RECIST 1.1)

Table 3: Most frequent (>10%) treatment-emergent AEs

Table 4: Treatment exposure

Efficacy results

Table 5: Best tumoral response by tumor type (RECIST 1.1)

Clinical benefit rate (CBR), defined as the proportion of patients with CR, PR or SD reported as related to IPH5401 and durvalumab was reported at DL3.

One DAE (diarrhea) reported as related to IPH5401 treatment (2 fatigue, 1 white blood cell count decreased, 1 headache and 1 dry mouth). There was no grade 3-4 IPH5401-related NCI CTCAE grade 3 or 4 toxicity in any patient.

Inhibiting C5aR signaling shown to increase CDT cell infiltration & function

One prolonged SD (40 weeks) reported in a HCC patient with prior progression after nivolumab. One prolonged SD (24 weeks) reported in a HCC patient with prior progression after nivolumab.

Clinical benefit rate (CBR), defined as the proportion of patients with CR, PR or SD at or below key secondary endpoints assessed (24% IPH5401 DL4 vs. 20% Nivolumab + Durvalumab).

One prolonged SD (40 weeks) was reported in a HCC patient with prior progression after nivolumab. This patient opted out of the study at DL3.

There was no DLT reported.

Twelve DAEs were reported among the 14 patients treated (Table 2) of which 12 were serious (grade 3-4).

Stable disease

Primary objective:

- To evaluate the safety of IPH5401 alone and in combination with durvalumab in advanced NSCLC patients (Astra Zeneca internal data)

Table 6: Number of patients treated

Table 1: C5 and C5ar1 expression in NSCLC IO-treated patients (RNAseq)

Table 2: Categorical data at baseline

Stable disease 3 1 0 1 5

One confirmed PR reported in a HCC patient with prior progression after nivolumab.

One prolonged SD (24 weeks) reported in an NSCLC patient with prior progression after nivolumab.

Clinical benefit rate (CBR), defined as the proportion of patients with CR, PR or SD at or below key secondary endpoints assessed (24% IPH5401 DL4 vs. 20% Nivolumab + Durvalumab).

Conclusion

• The combination of IPH5401 and durvalumab was well tolerated, no DLT was reported and no dose relationship could be observed regarding safety.

• Encouraging early efficacy signals were observed in HCC and NSCLC.

• Pharmacodynamic analyses confirmed the full receptor saturation at all dose levels and the absence of impact on neutrophil counts.

• STELLAR-001 study is now moving to next step with expansion cohorts in IO-pretreated NSCLC and IO-naïve HCC to generate additional safety and efficacy data as well as translational analyses on tumor biomarkers.

Table 2: Categorical data at baseline

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