Phase 1 trial of MOv18, a first-in-class IgE antibody therapy for cancer

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Background

- all antibodies approved for the treatment of cancer are monoclonal IgGs
- IgE biology, compared with IgG, offers potential for enhanced immune surveillance and superior effector cell potency against tumors:
  - very high affinity for FcɛRs
  - receptors expressed on tissue-resident effector cell types
  - no inhibitory Fc receptor for IgE
- no IgE therapy previously tested in humans
- first GMP manufacture of IgE
- total starting dose = 70µg

PBS  IgG  IgE


- immunocompetent rat model
- syngeneic tumor expressing FRα
- efficacy assessed from number and density of pulmonary metastases
- no allergic tox
Study design and safety mitigation

Eligible patients:
- advanced FRα+ solid tumours
- adequate organ function
- no history of severe allergy
- absence of concomitant drugs or comorbidities increasing risk in event of anaphylaxis

Trial schema:
- 6x weekly infusions
- CT response assessment
- 3x 2-weekly maintenance infusion
- Off study & follow-up

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Dose level</th>
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<tbody>
<tr>
<td>1</td>
<td>70 µg</td>
</tr>
<tr>
<td>2</td>
<td>250 µg</td>
</tr>
<tr>
<td>3</td>
<td>500 µg</td>
</tr>
<tr>
<td>4</td>
<td>700 µg</td>
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<tr>
<td>5</td>
<td>1.5 mg</td>
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<tr>
<td>6</td>
<td>3 mg</td>
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24 patients treated to date

i) skin prick testing pre-IV dosing

ii) basophil activation test (BAT) pre-IV dosing

Bax et al. *Allergy* 2020

Fold change in CD63

Cancer Research UK
Safety

Treatment-related AEs:

- Anaphylaxis in single patient at 500µg
  - clinical features; serum tryptase elevation
  - interpretation of positive BAT at baseline
    - prevalence in population
  - subsequently, BAT+ = exclusion criterion
Pharmacokinetics; ADA

Pharmacokinetics:

- Cohort 5
- Cohort 4
- Cohort 3
- Cohort 2
- Cohort 1

Mean $t_{1/2} = 9.2$ hours

Anti-drug antibody: ADA detected in 3*/22 evaluable patients at 6 weeks and/or at off study follow up (>8 weeks)

* 1 ADA is suspected: data under review

Anti-tumor activity

Patient 10/019: 700µg. Measurable response not RECIST PR

CA125 (U/ml)

Cohort 1
Cohort 2
Cohort 3
Cohort 4
Cohort 5

Pharmacokinetics:

MOv18 (ng/mL)

Hours

0 10 20 30 40

0 50 100

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**Conclusions**

- IgE biology is well suited for anti-cancer therapy
- administration is tolerable in most patients; single episode of anaphylaxis:
  - resolved quickly with standard management
  - successful mitigation using baseline BAT for all subsequent patients
- evidence of transient anti-tumor activity at 700 µg
- dose escalation continues
- these results support for the first time the safety and potential efficacy of IgE as a treatment for cancer
- clinical testing of class-switched IgE versions of approved IgG drugs seems warranted

Pellizzari G et al. EBioMedicine (2019)
Acknowledgements and disclosure

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JS and SK are co-founders of IGEM Therapeutics Ltd. HB is employed through a fund from IGEM Therapeutics Ltd. SK holds a patent on anti-tumour IgE antibodies

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