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

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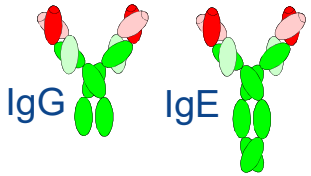
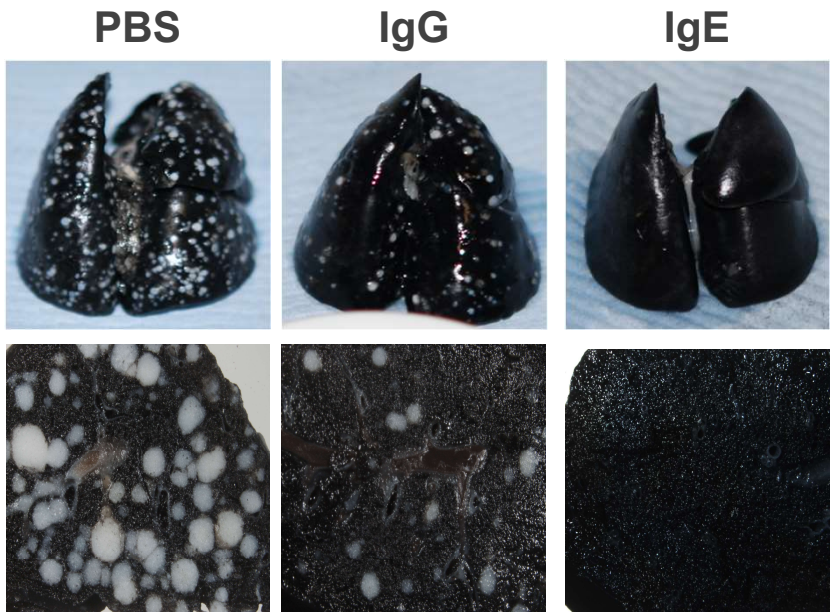
Background

- 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 FcεRs
  - 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



Josephs D et al. *Cancer Res* (2017)

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

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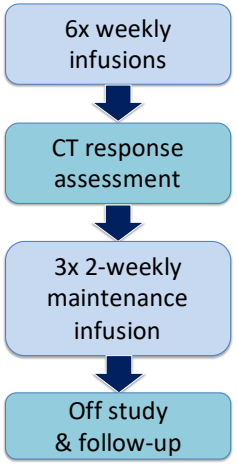
Study design and safety mitigation

Eligible patients:

- advanced FRα+ solid tumours
- adequate organ function
- no history of severe allergy
- absence of conmeds or comorbidities increasing risk in event of anaphylaxis

Trial schema:

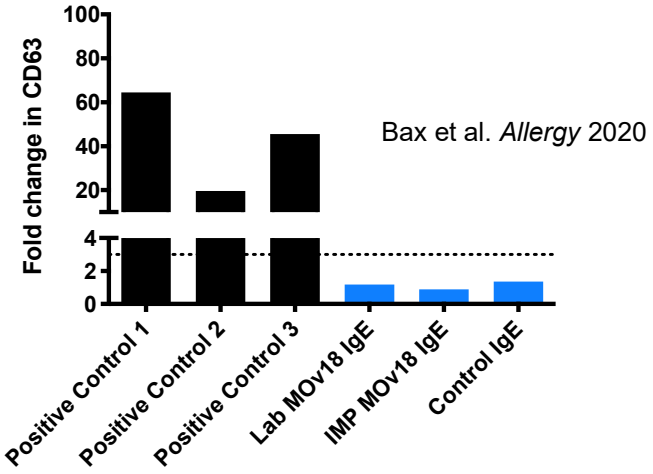


24 patients treated to date

Cohort	Dose level
1	70 µg
2	250 µg
3	500 µg
4	700 µg
5	1.5 mg
6	3 mg

i) skin prick testing pre-IV dosing

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



Bax et al. *Allergy* 2020

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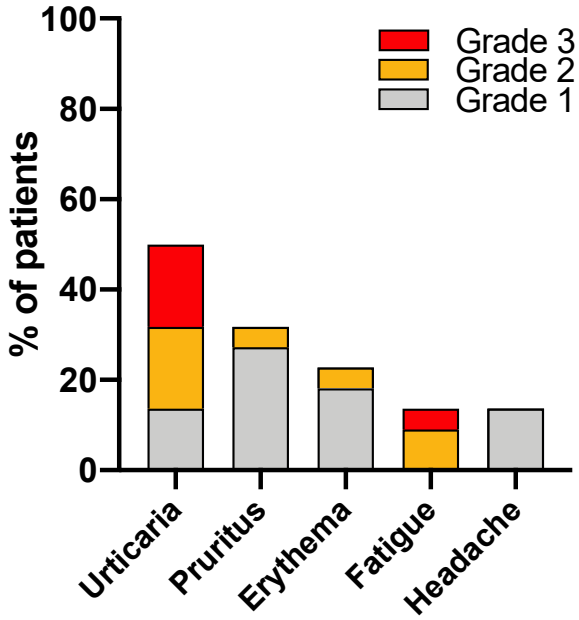
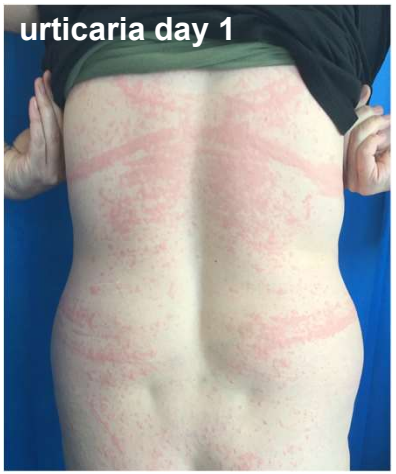
Safety

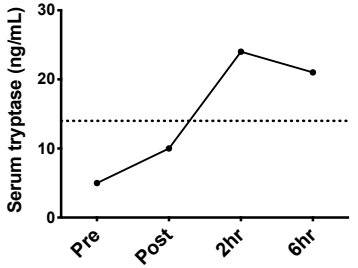
Treatment-related AEs:



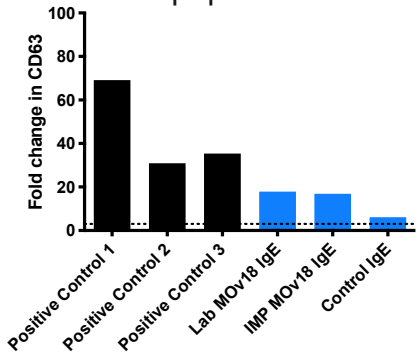


Anaphylaxis in single patient at 500µg

- clinical features; serum tryptase elevation



- interpretation of positive BAT at baseline
  - prevalence in population



- subsequently, BAT+ = exclusion criterion

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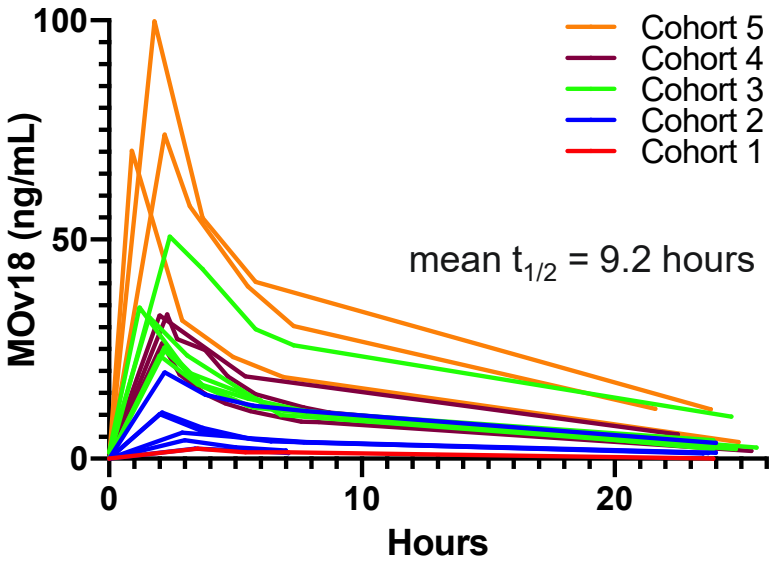
Pharamcokinetics; ADA

Pharmacokinetics:

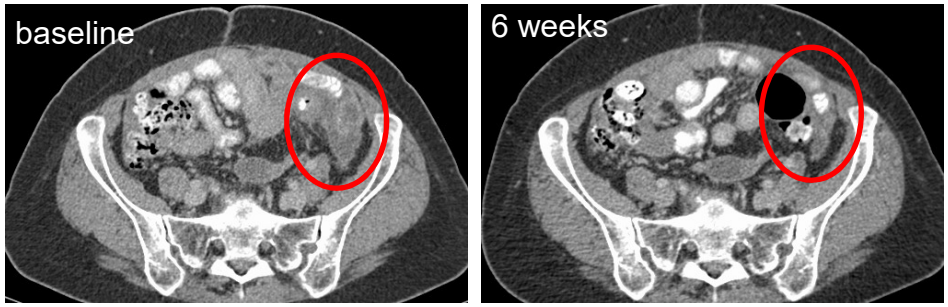


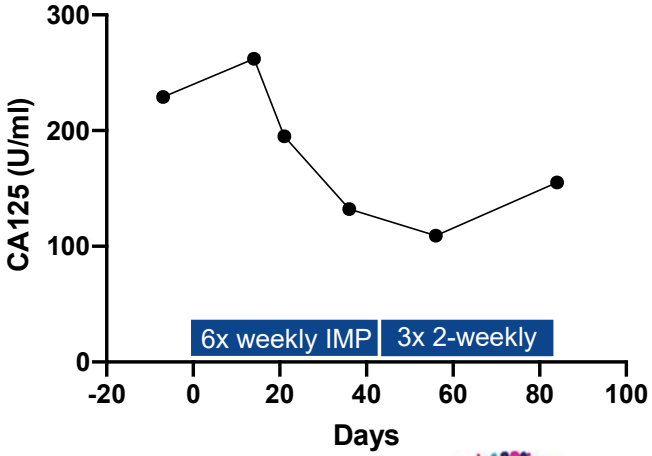
Anti-drug antibody: ADA detected in 3*/22 evaluable patients at 6 weeks and/or at off study follow up (>8 weeks)

* 1 ADA is suspected: data under review

Anti-tumor activity

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





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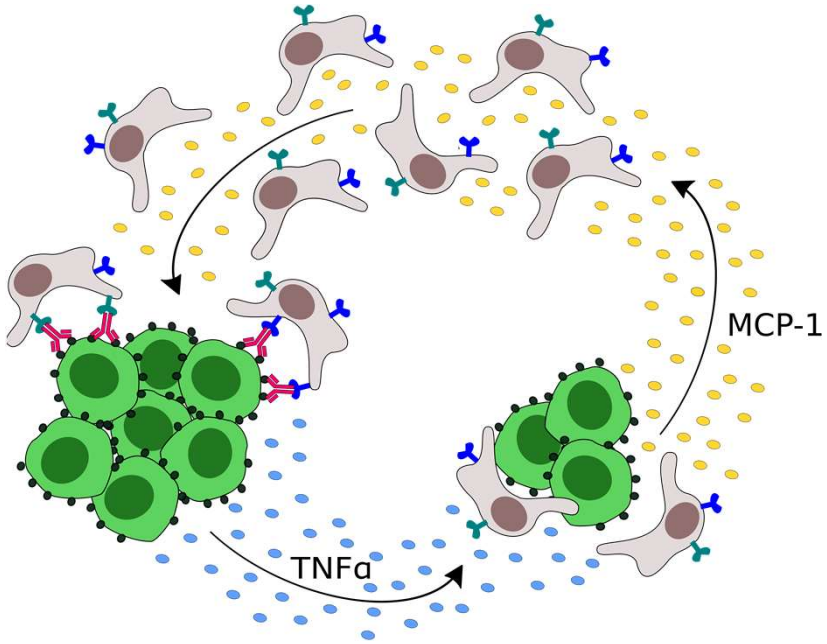
Conclusions

- 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



Josephs D et al. *Cancer Res* (2017)
Pellizzari G et al. *EBioMedicine* (2019)

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ecmc

Fondazione IRCCS Istituto Nazionale dei Tumori

OHCT Oncology & Haematology Clinical Trials

MRC Medical Research Council

NHS National Institute for Health Research

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