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First-in-human study with intratumoral administration of a CD40 agonistic antibody: Preliminary results with ADC-1013/JNJ-64457107 in advanced solid malignancies

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Presenter Disclosure Information

Peter Ellmark

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I am employed by Alligator Bioscience and hold stocks and stock options in Alligator Bioscience

Presentation Slides

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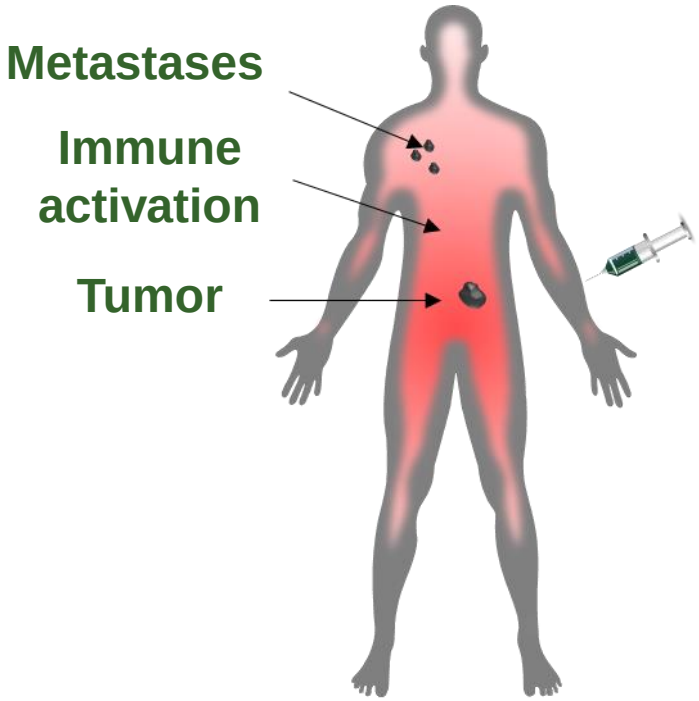
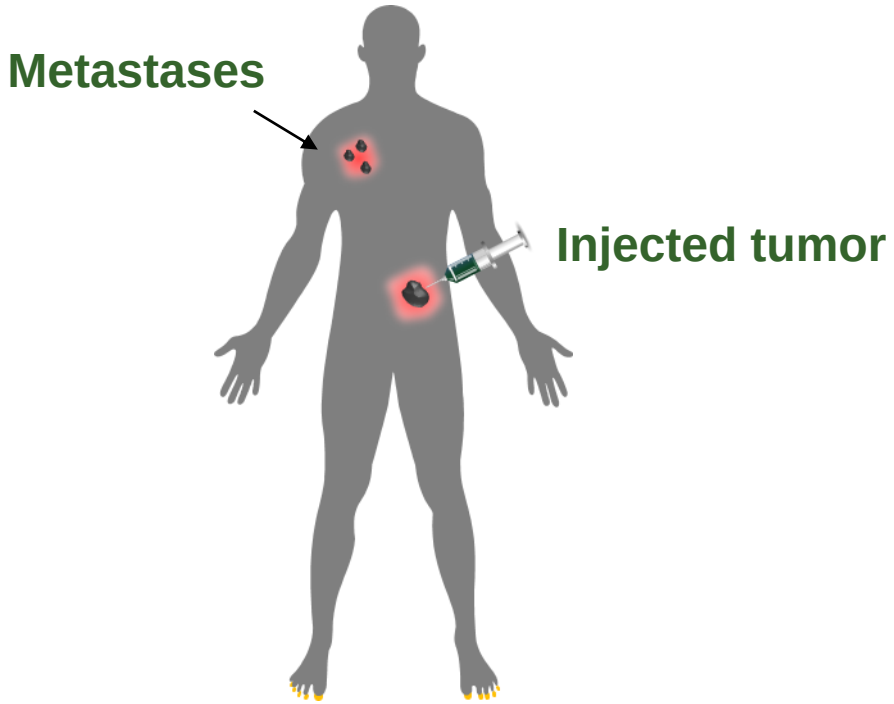
Tumor-directed immuno-oncology



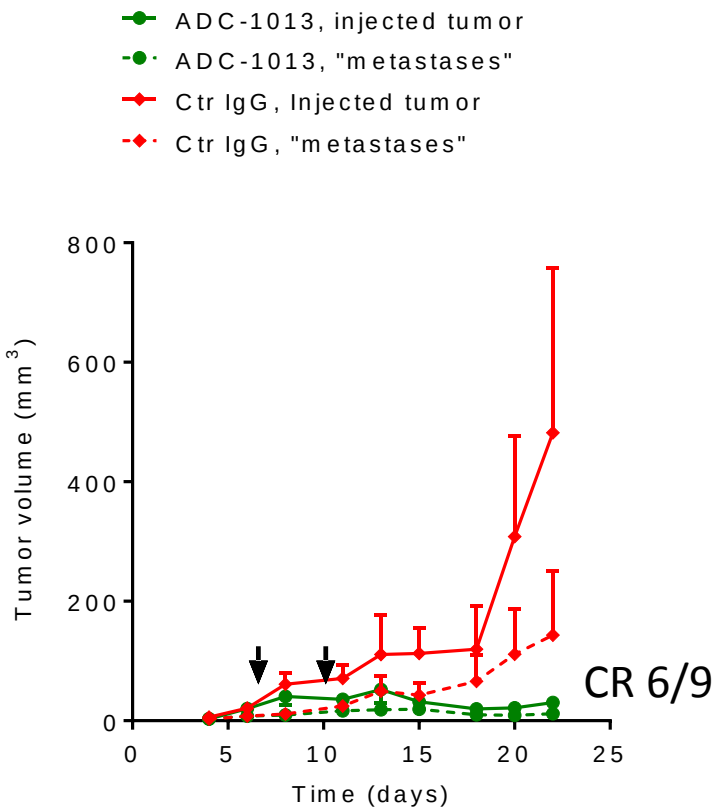
GENERAL IMMUNE-ACTIVATION



TUMOR-DIRECTED IMMUNE-ACTIVATION

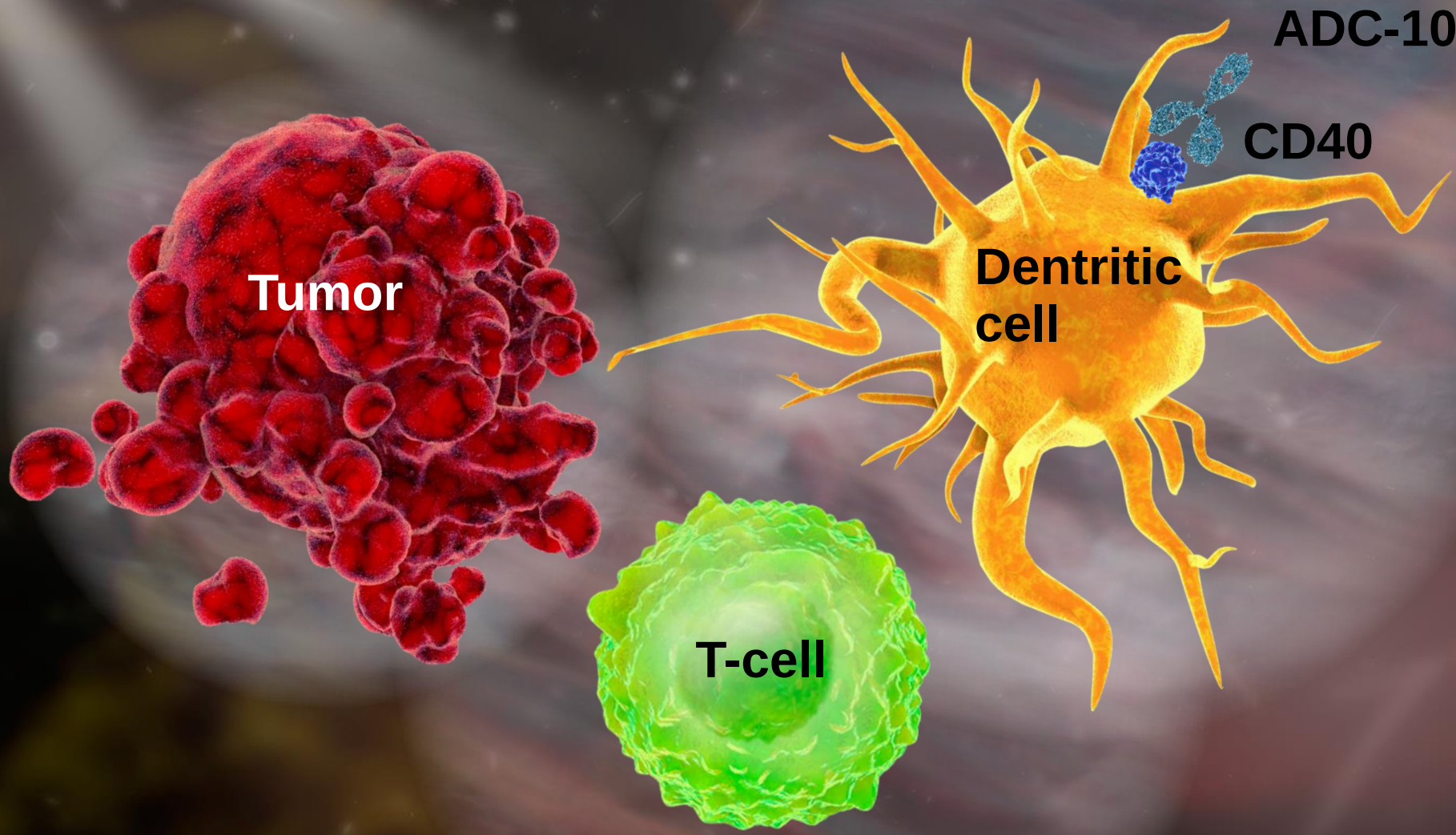
Adapted from Ellmark *et al* 2016, CII

Supported by pre-clinical data:



Adapted from Mangsbo *et al* 2015, CCR

CD40 is a key immuno-oncology target



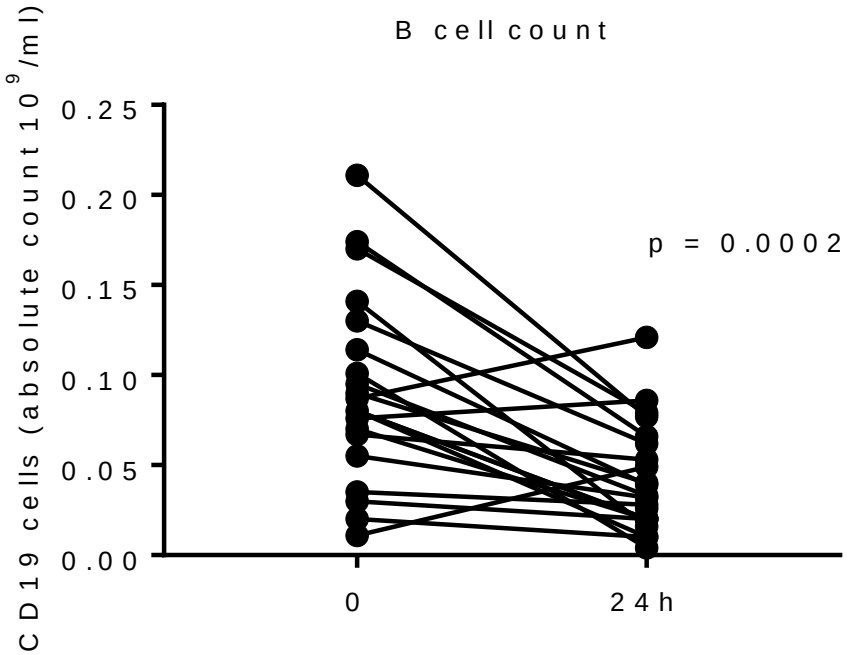
First-in-human clinical phase 1 (NCT02379741)

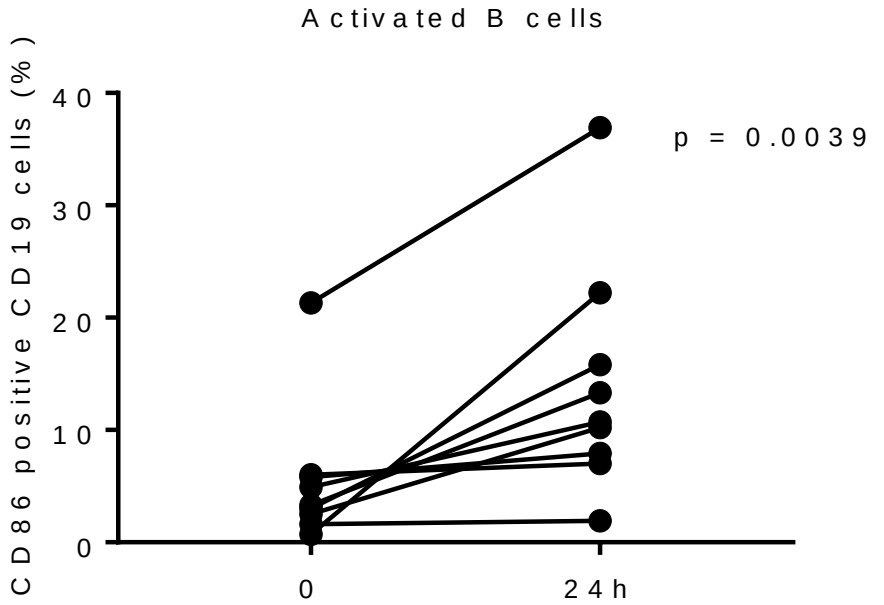
- Study therapy: ADC-1013 intratumoral (or IV) every 14 days
- Study design: ADC-1013 dose escalation in subjects with advanced stage solid tumors to evaluate safety and tolerability
- Status:
  - 1st patient dosed April, 2015
  - Five clinical centers in Sweden, Denmark and UK
  - Study completed, 24 subjects enrolled

Demographics

Administration route	Intratumoral				IV
Dose level (µg/kg)	22.5	75	200	400	75
Number of patients dosed	3	4	3	8	5
Age median (years)	67.0	62.5	74.0	59.0	60.0
Sex: Male/Female	3/0	2/2	2/1	3/5	4/1
Tumor type					
Colon/Rectal cancer		1	3	3	2
Melanoma	1			1	
Kidney	2			2	
Bile duct				1	1
Breast				1	
Ovarian		1			
Lung Cancer		2			
Peritoneal Cancer					1
Oesophageal Cancer					1

ADC-1013 mediates CD40 agonistic responses in advanced stage cancer patients





Treatment related adverse events ≥ grade 3

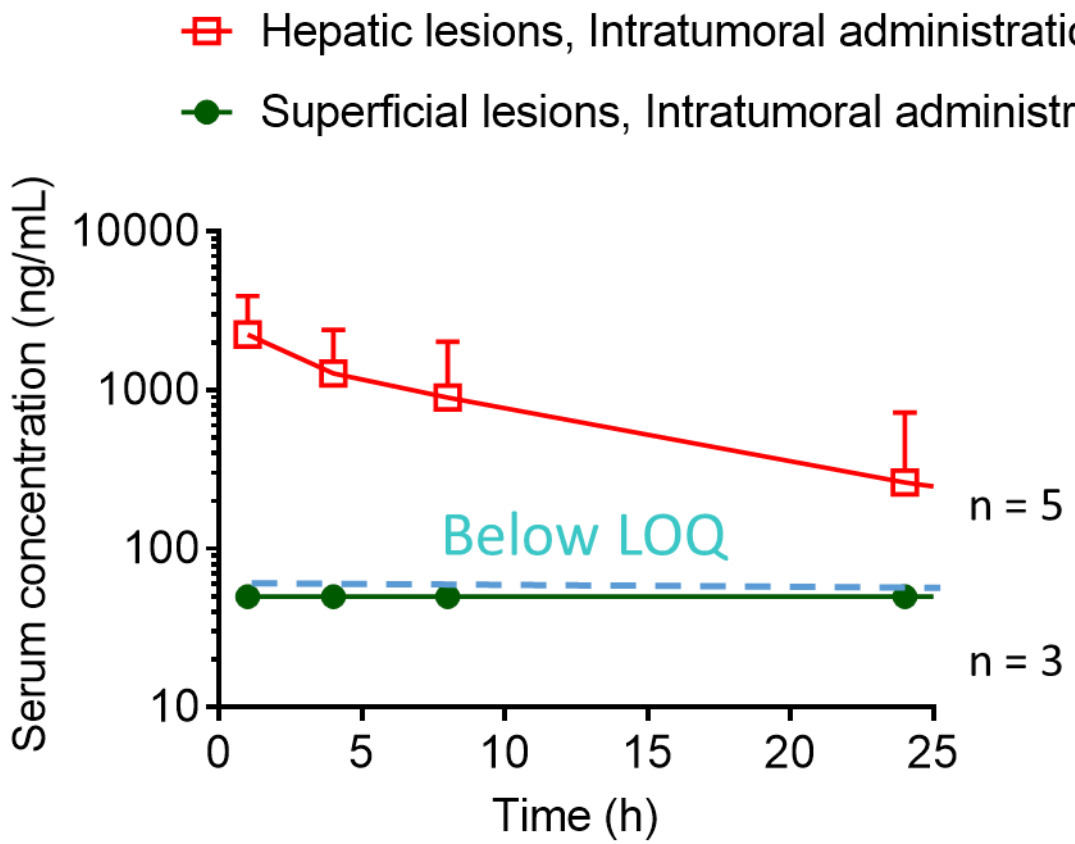
- majority of adverse events were grade 1 and 2 and transient

Drug-related adverse events ≥ grade 3	Pat ID	Dose level (µg/kg)	Grade	Dose limiting toxicity
Chills	009	200	3	No
Hypotension	011	400	3	No
Cholecystitis	014	400	3	Yes
Shiverings	016*	400	3	No
Abdominal pain	016	400	3	Yes

* At two occasions

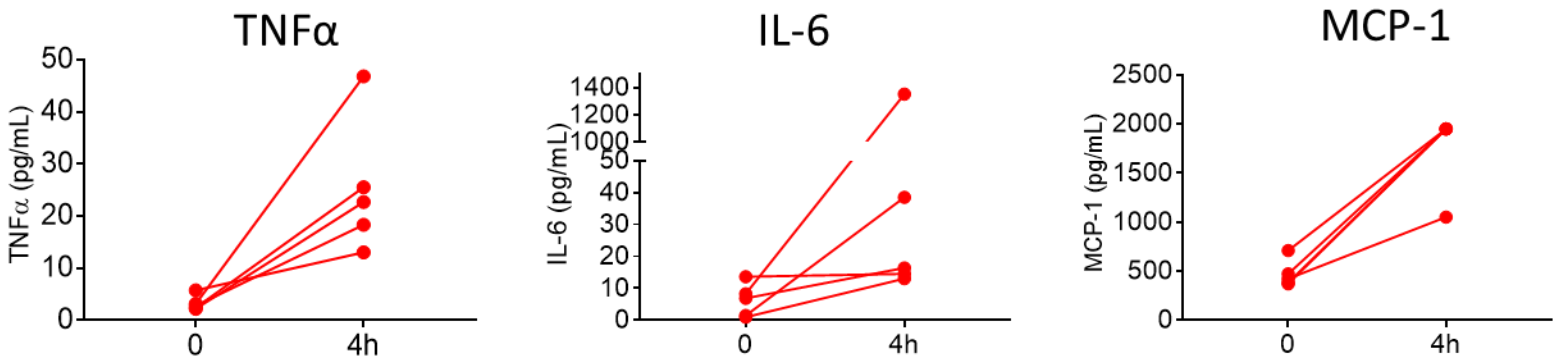
Serum concentration of ADC-1013 (400 µg/kg dose)

- low systemic exposure following injections into superficial lesions

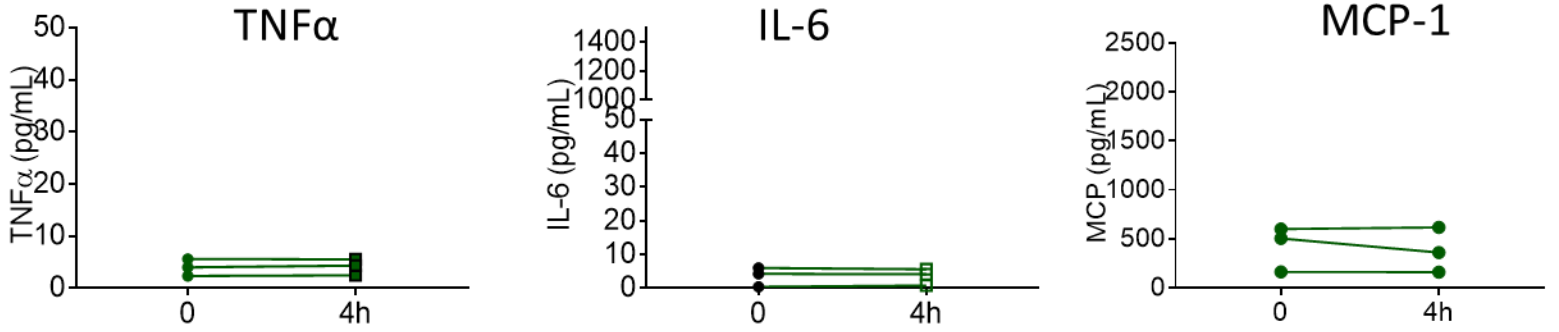


Early cytokine release only detected following hepatic injection of ADC-1013 (400 µg/kg dose level)

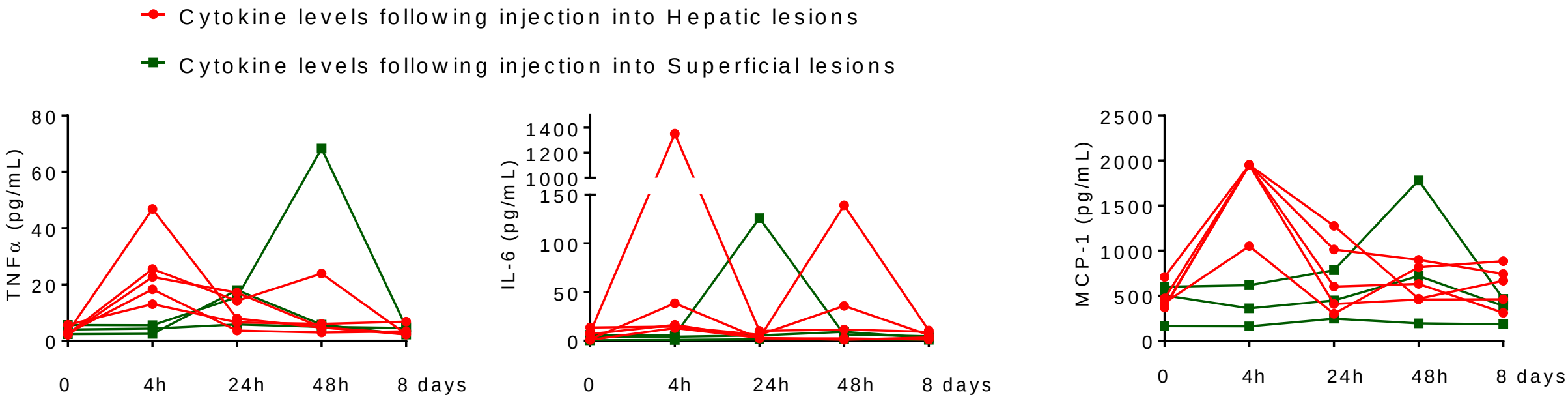
Injections into hepatic lesions



Injections into superficial lesions

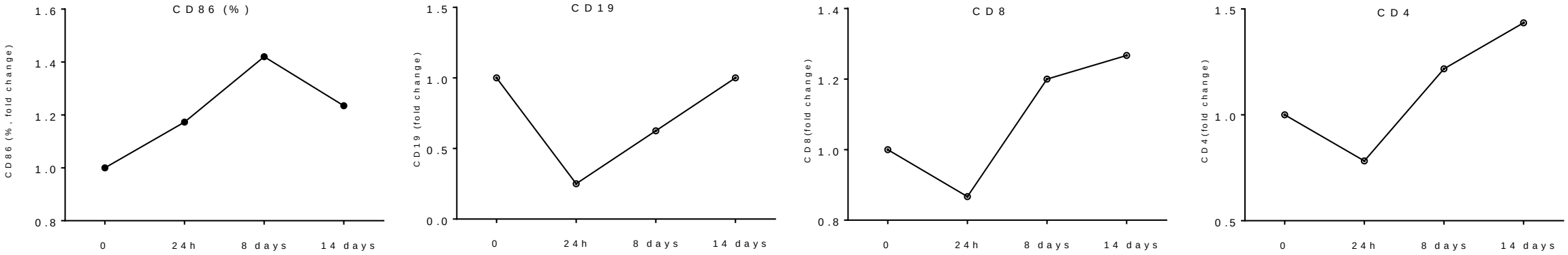


ADC-1013-mediated cytokine release over time following the first dose (400 µg/kg dose level)



Tumor effects – case study (Patient ID 015)

- Best response in study: Stable disease (12 months on study)
- Male 57 year, metastatic kidney cancer
- 7 treatment cycles: 400 µg/kg, 600 µg/kg and 900 µg/kg, no severe AE
- Indication of pharmacodynamic responses, including B cell activation



Lessons and Take Home Messages

- ADC-1013 induces CD40-mediated pharmacodynamics effects
- Injection into superficial lesions results in low systemic exposure, but with indications of systemic pharmacodynamic responses
- Intratumoral administration is well tolerated in superficial lesions at least up to 400 µg/kg (MTD 200 µg/kg in hepatic lesions)

Current development, Janssen Phase 1 study (NCT02829099)

- **Study Therapy:** JNJ-64457107 (ADC-1013) IV every 14 days (75 µg/kg starting dose)
- **Study design:**
  - Part 1: JNJ-64457107 (ADC-1013) dose escalation in subjects with advanced stage solid tumors
  - Part 2: JNJ-64457107 (ADC-1013) dose expansion: NSCLC, pancreatic cancer, and cutaneous melanoma.
- **Status:**
  - 1st patient dosed on October 26, 2016
  - Currently 52 subjects enrolled

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Participating patients

Meet us at Poster: O24

Serum concentration of ADC-1013 (400 µg/kg dose)

- low systemic exposure following injections into superficial lesions