# Webinar Outline

- A Phase 2, Multi-Center Study of the Safety and Efficacy of Tebentafusp in Patients with Metastatic Uveal Melanoma (IMCgp100-102) - **Joseph Sacco, MBChB, MSc, MRCP, PhD**
- A phase I clinical trial on intratumoral administration of ipilimumab plus nivolumab followed by intracavitary administration of nivolumab in patients with recurrent glioblastoma - **Julia Katharina Schwarze, MD, MSc**
- Additional clinical abstracts of interest from ESMO IO 2020 - **Sunandana Chandra, MD, MS**

# Additional clinical abstracts of interest

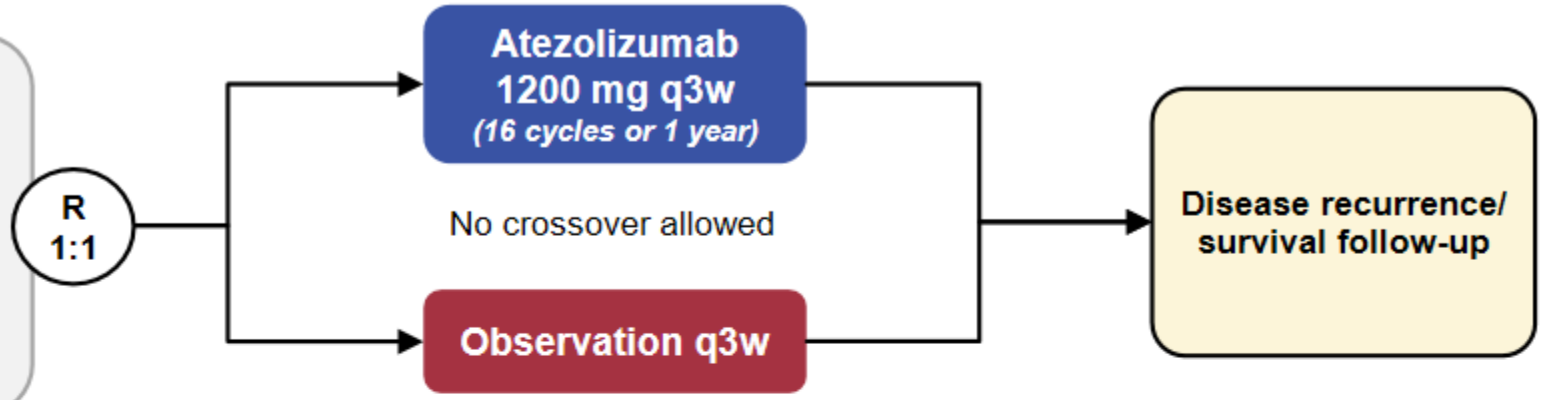
- Abstract 1: Clinical outcomes in post-operative ctDNA(+) muscle-invasive urothelial carcinoma patients after atezolizumab adjuvant therapy – *Thomas Powles*
- Abstract 2: TG4001 therapeutic vaccination combined with PD-L1 blocker avelumab remodels the tumor microenvironment (TME) and drives antitumor responses in human papillomavirus (HPV)+ malignancies – *C. Le Tourneau*
- Abstract 3: A randomized, controlled, multicenter phase II trial of camrelizumab combined with albumin-bound paclitaxel and cisplatin as neoadjuvant treatment in locally advanced NSCLC – *Jie Lei*

# Clinical outcomes in post-operative ctDNA(+) muscle-invasive urothelial carcinoma patients after atezolizumab adjuvant therapy

Thomas Powles, Zoe June Assaf, Nicole Davarpanah, MahaHussain, Stephane Oudard, Jürgen E. Gschwend, Peter Albers, Daniel Castellano, Hiroyuki Nishiyama, SiamakDaneshmand, Petros Grivas, Shruti Sharma, Himanshu Sethi, Alexey Aleshin, JingbinZhang, Viraj Degaonkar, Carlos Bais, Corey A. Carter, Joaquim Bellmunt, Sanjeev Mariathasan

# IMvigor010: Trial design

**Key eligibility**
- High-risk MIUC (bladder or upper tract)
- Radical surgery with lymph node dissection within ≤14 weeks
- Tissue sample for PD-L1 testing




**Endpoints**
- Primary: DFS (ITT population)
- Key secondary: OS (ITT population)
- Other: Safety
- **Exploratory: predictive, prognostic and pharmacodynamic biomarkers in tumour tissue and blood and their association with disease recurrence**

- IMvigor010 did not meet its primary endpoint (DFS in the ITT population)[1]
  - A pre-planned interim OS analysis was performed but could not be formally tested
  - OS follow-up is immature and ongoing in the ITT population
- The PD-L1 and TMB biomarkers did not identify patients benefitting from atezolizumab vs observation in the ITT population
- A pre-specified ctDNA biomarker analysis was performed using the Signatera assay

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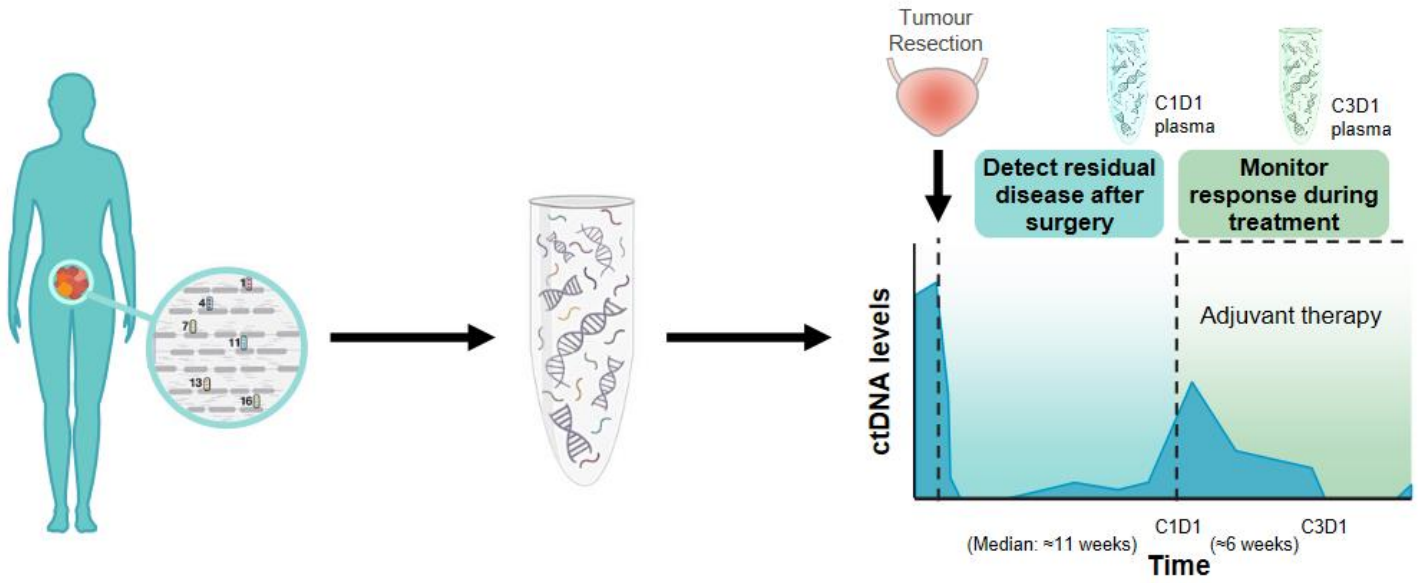
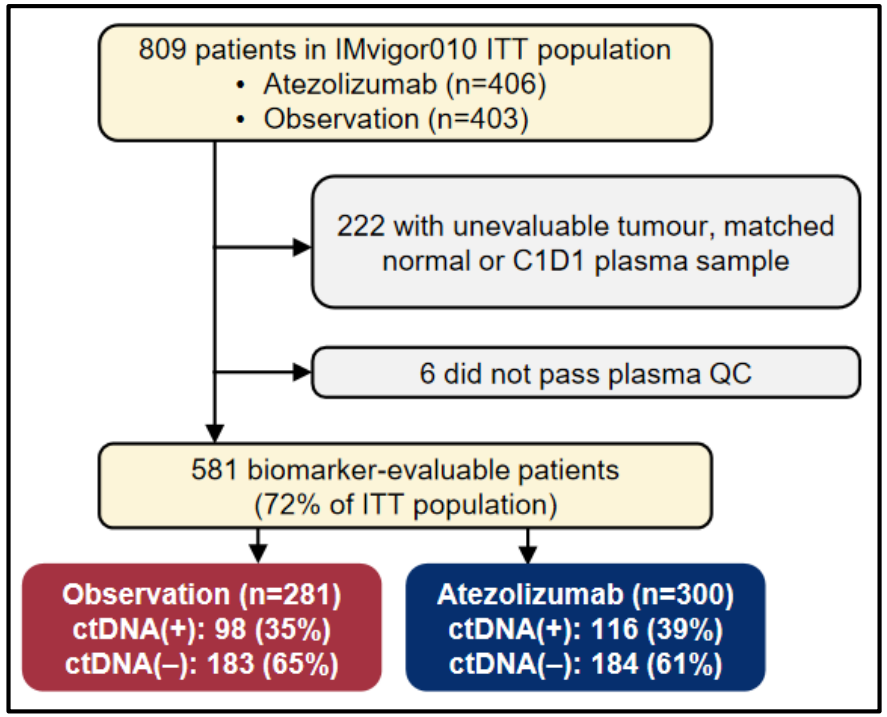
# ctDNA evaluation in IMvigor010

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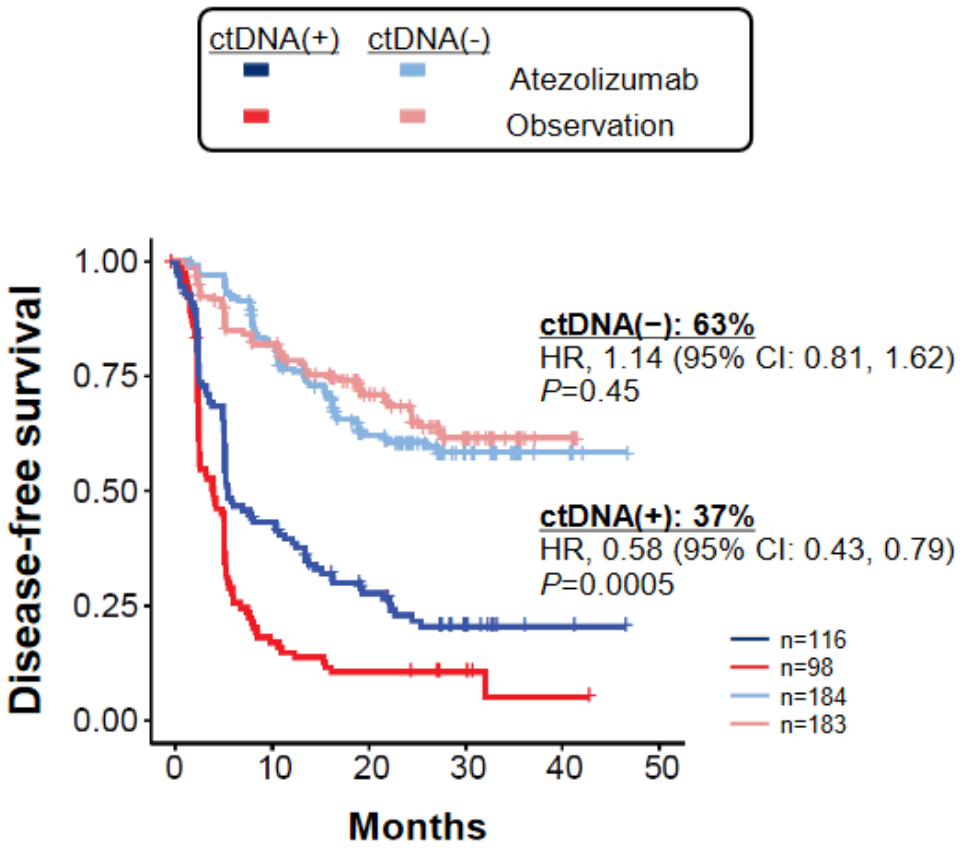
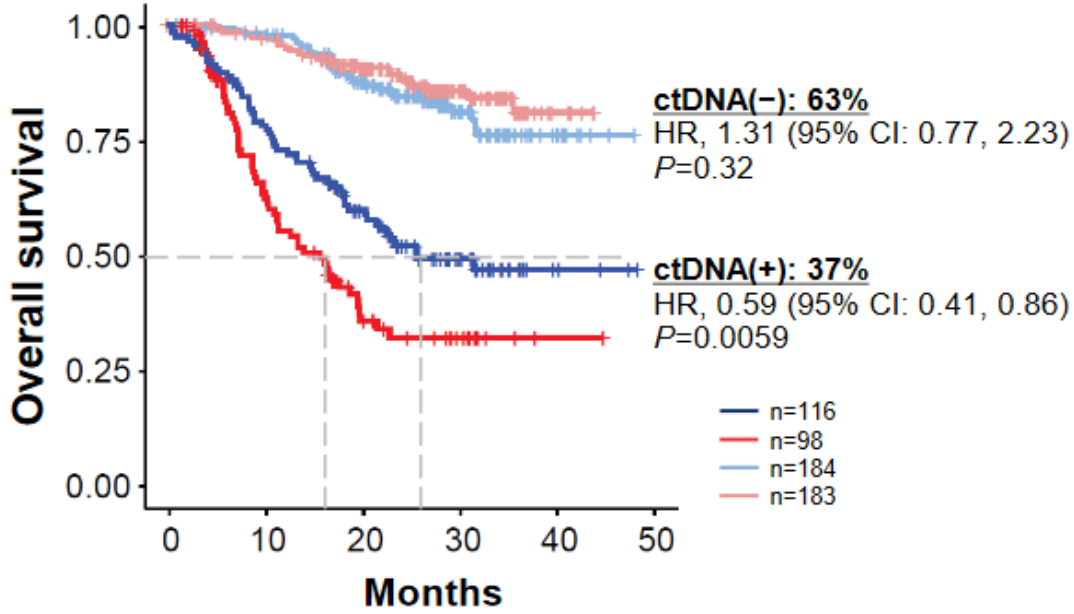
# ctDNA(+) patients had improved outcomes with atezolizumab treatment

| | ctDNA(+) patients | |
|---|---|---|
| | Atezolizumab | Observation |
| Median DFS (95% CI), mo | 5.9 (5.6, 11.2) | 4.4 (2.9, 5.6) |
| Median OS (95% CI), mo | 25.8 (20.5, NR) | 15.8 (10.5, 19.7) |

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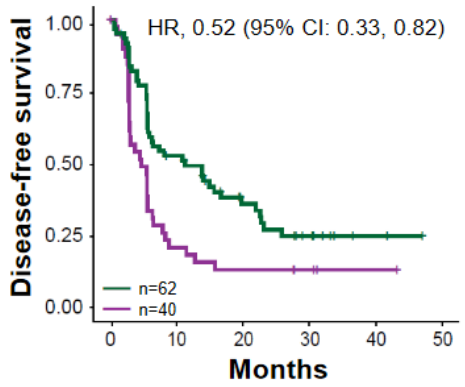
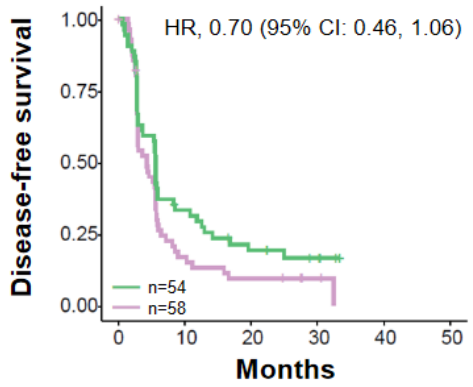
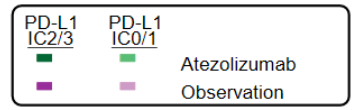
# PD-L1(+) or TMB-high, ctDNA(+) patients have improved outcomes with atezolizumab

ctDNA(+): PD-L1 IC2/3

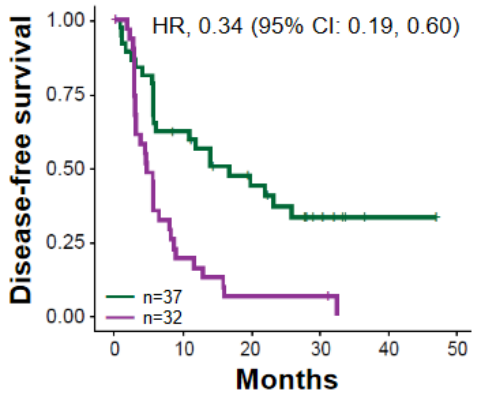



PD-L1 IC0/1

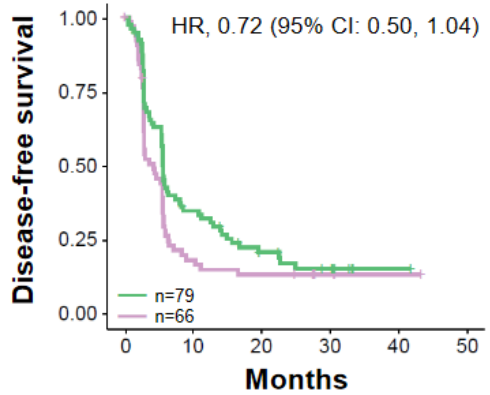


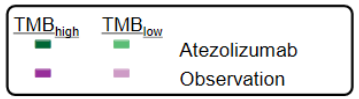




ctDNA(+): $TMB_{high}$




$TMB_{low}$

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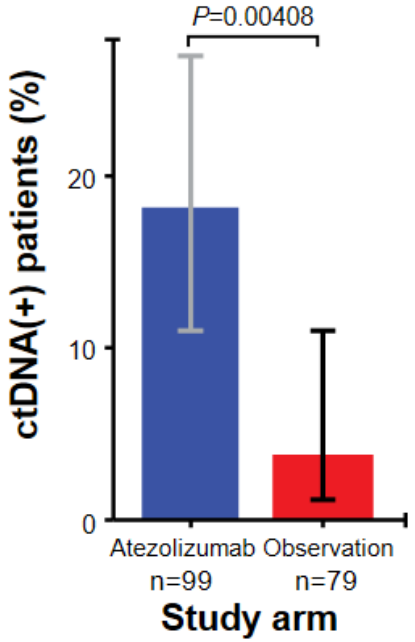
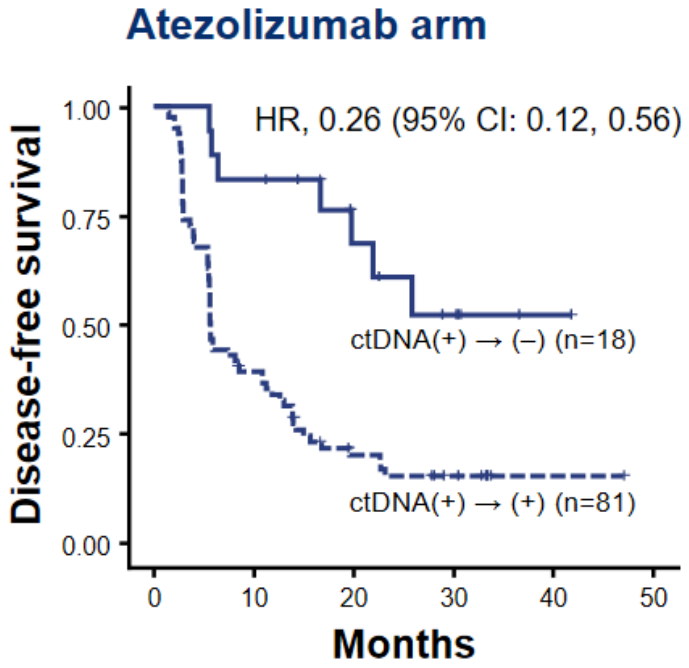
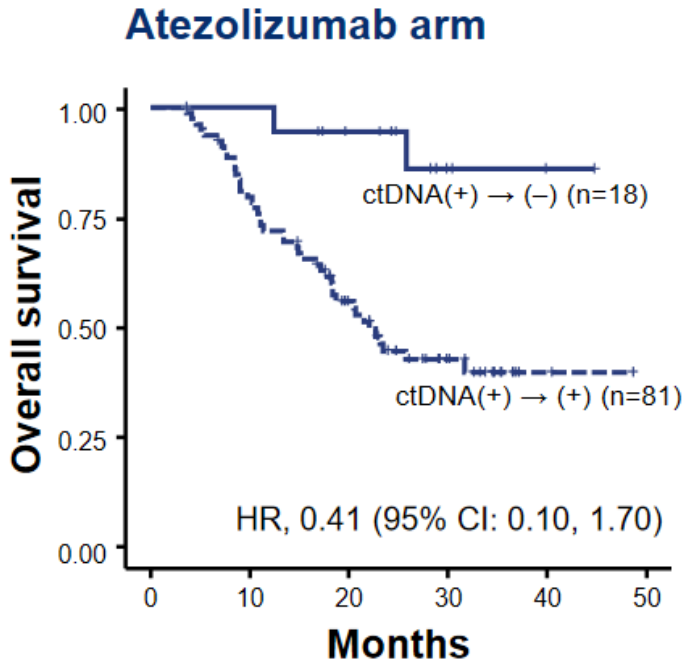
# ctDNA clearance associated with improved outcomes with atezolizumab




| | | |
|---|---|---|
| ctDNA(+) → (–) | 18 (18.8%) | 3 (3.8%) |
| ctDNA(+) → (+) | 81 (81.82%) | 76 (96.2%) |

- ctDNA clearance occurs at a higher rate in the atezolizumab vs observation arm (C1 → C3)




- ctDNA clearance was associated with improved DFS and OS outcomes in the atezolizumab arm

Powles, ESMO-IO 2020

# TG4001 therapeutic vaccination combined with PD-L1 blocker avelumab remodels the tumor microenvironment (TME) and drives antitumor responses in human papillomavirus (HPV)+ malignancies

C. Le Tourneau, P. Cassier, F. Rolland, S. Salas, J.-M. Limacher, O. Capitain, O. Lantz, A. Lalanne, C. Ekwegbara, A. Tavernaro, H. Makhloufi, K. Bendjama, J.-P. Delord

# Study design and patient characteristics

**Key Eligibility Criteria**

- Metastatic or refractory/recurrent HPV-16+ cancer including oropharyngeal SCCHN, cervical, vulvar, vaginal, penile and anal cancer
- HPV16 positivity determined in central laboratory by nested PCR with HPV-16 specific probes and retest of negative results by sequencing
- Up to two prior lines of systemic therapy for the management of metastatic or recurrent disease
- ECOG PS 0 or 1
- No previous exposure to cancer immunotherapies
- No CNS metastases
- No chronic treatment with systemic corticosteroids

**Treatment regimen**

**TG4001: administered SC**

- Weekly for 6 weeks, then every 2 weeks up to M6, and every 12 weeks

**Avelumab: 10mg/kg – administered IV**

- Every 2 weeks starting one week after the first vaccine dose

**Pooled analysis of phase Ib/II consisting of 6 patients of the phase Ib treated with the phase II dose of TG4001 = $5x10^7$ pfu and 28 evaluable patients of the phase II**

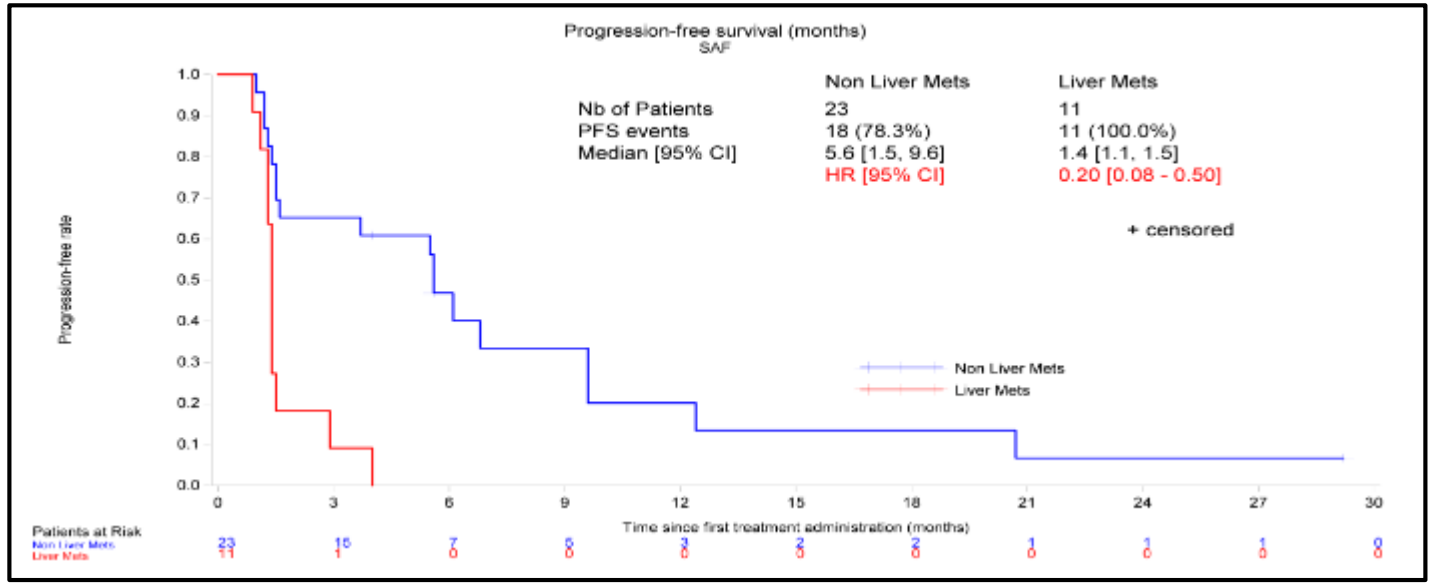
**Patient Demographics and Baseline Characteristics**

| | Phase I (n=6) | Phase II (n=28) | Overall (N=34) |
|---|---|---|---|
| **Age (years)** | | | |
| Mean | 61.2 | 58.3 | 58.8 |
| Range | 39 - 78 | 28 - 79 | 28 - 79 |
| **Gender** | | | |
| Female | 2 | 20 | 22 (64.7%) |
| Male | 4 | 8 | 12 (35.3%) |
| **Performance Status (ECOG)** | | | |
| 0 | 4 | 10 | 14 (41.2%) |
| 1 | 2 | 18 | 20 (58.8%) |
| **Primary tumor** | | | |
| Anal | 0 | 15 | 15 (44.1%) |
| Cervical | 1 | 5 | 6 (17.6%) |
| Oropharyngeal | 4 | 4 | 8 (23.5%) |
| Vaginal | 1 | 3 | 4 (11.8%) |
| Vulvar | 0 | 1 | 1 (2.9%) |
| **Number of organs Involved** | | | |
| 1 | 3 | 9 | 12 (35.3%) |
| 2 | 2 | 11 | 13 (38.2%) |
| 3 | 1 | 8 | 9 (26.5%) |
| **Number of CT lines for R/M disease** | | | |
| 0 | 2 | 2 | 4 (11.8%) |
| 1 | 4 | 15 | 19 (55.9%) |
| 2 | 0 | 11 | 11 (32.3%) |
| **Tumor burden (mm)** | | | |
| Mean | 47.0 | 70.4 | 66.3 |
| Median | 46.5 | 61.4 | 58.5 |
| Range | 28.0 – 72.0 | 11.0 – 199.0 | 11.0 – 199.0 |

Le Tourneau, ESMO-IO 2020

# Efficacy of TG4001 and avelumab

| Efficacy parameters | Patients without liver metastases n=23 | Patient with liver metastases n=11 | Overall n = 34 |
|---|---|---|---|
| **Response (RECIST 1.1)** | | | |
| CR : Complete Response | 1 (4.3%) | 0 | 1 (2.9%) |
| PR : Partial Response | 7 (30.4%) | 0 | 7 (20.6%) |
| ORR : Overall Response | 8 (34.8%) [16.4 ; 57.3] | 0 (0%) | 8 (23.5%) [10.7 ; 41.2] |
| **Disease Control Rate (DCR)** at 12 weeks | 13 (56.5%) | 1 (9.1%) | 14 (41.2%) |
| **Progression ≤ 12 weeks** | 10 (43.5%) | 10 (90.9%) | 20 (58.8%) |
| Response according to primary tumor (responders/total number of patients %) : | | | |
| Anal | 2/7 (28.6%) | 0/8 | 2/15 (13.3%) |
| Oropharyngeal | 2/8 (25.0%) | - | 2/8 (25.0%) |
| Cervical | 2/5 (40.0%) | 0/1 | 2/6 (33.3%) |
| Vulvar/Vaginal | 2/3 (66.7%) | 0/2 | 2/5 (40.0%) |

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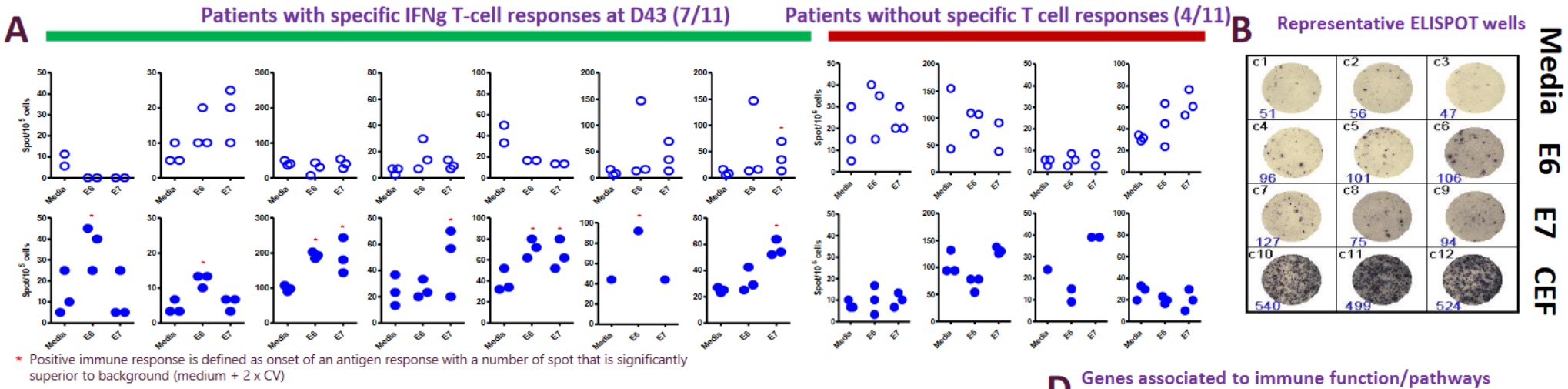
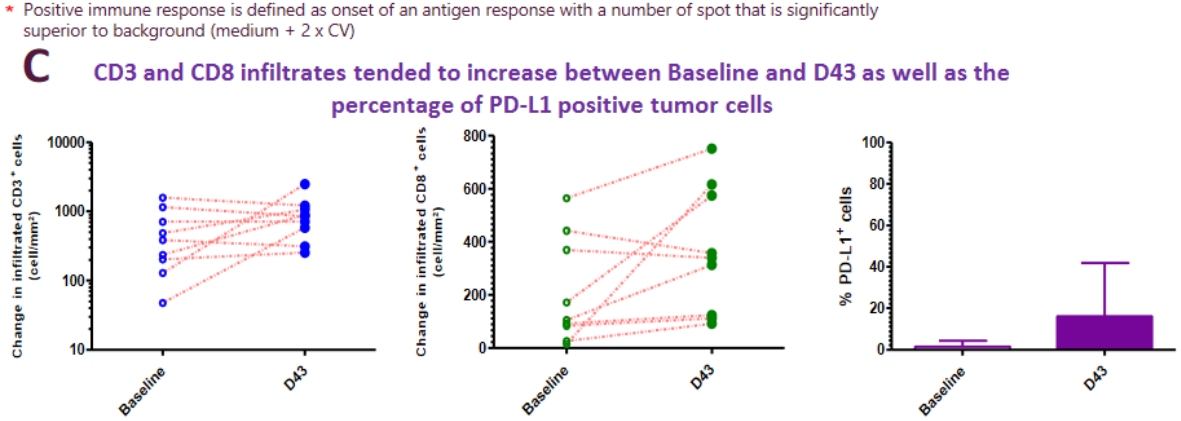
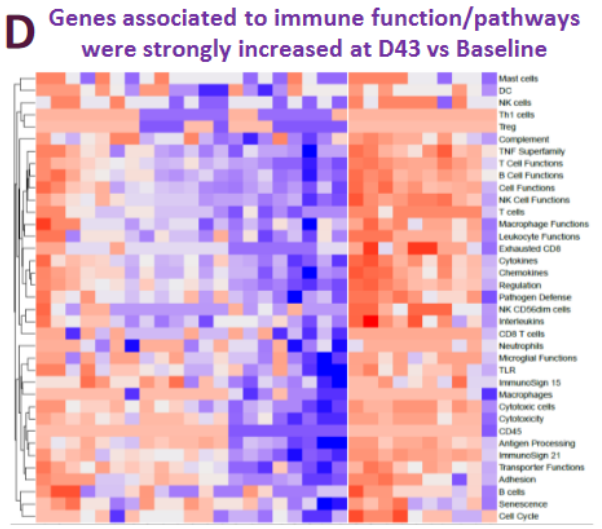
# Immune studies



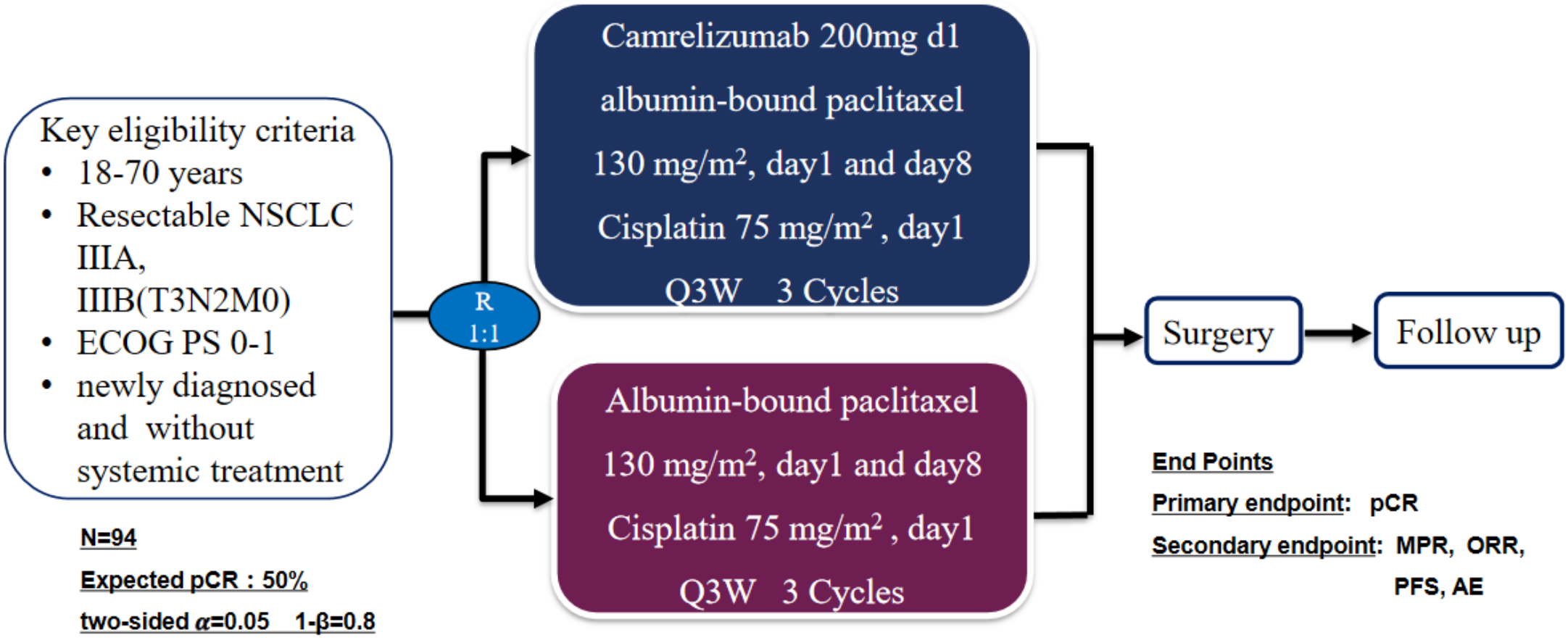



# A randomized, controlled, multicenter phase II trial of camrelizumab combined with albumin-bound paclitaxel and cisplatin as neoadjuvant treatment in locally advanced NSCLC

Jie Lei, Xiaolong Yan, Jinbo Zhao, Feng Tian, Qiang Lu, Tao Jiang

# Study design

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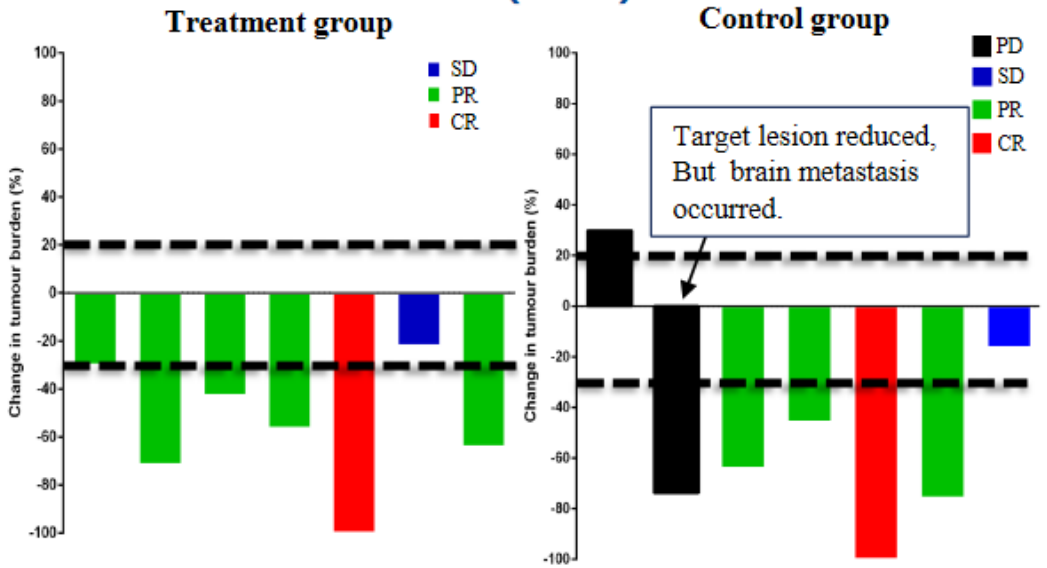
# Efficacy

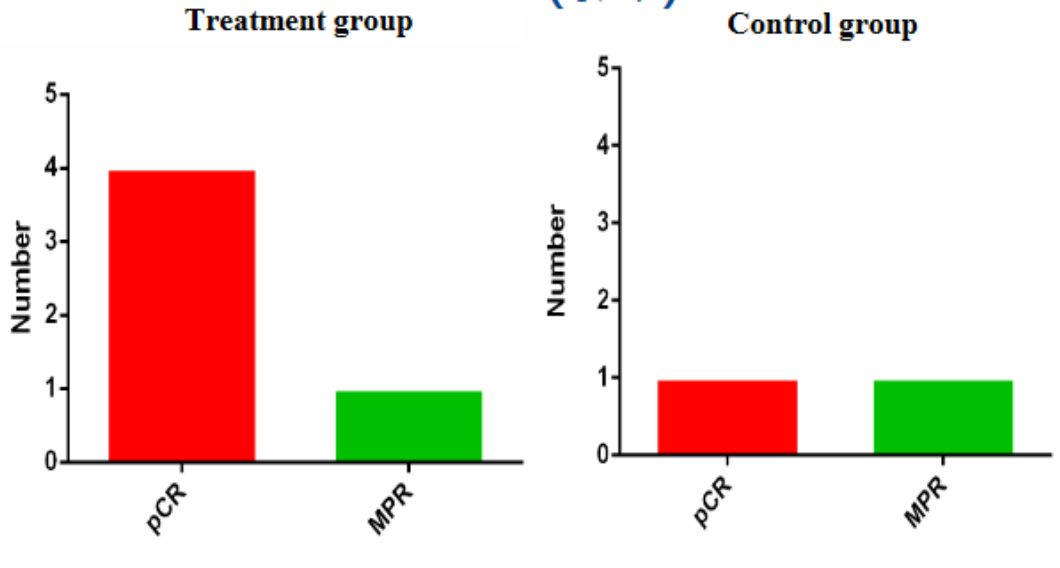
## Response according to RECIST 1.1 ( N=7 )




| Bset Response | N (7) | % |
|---|---|---|
| CR | 1 | 14.29 |
| PR | 5 | 71.42 |
| SD | 1 | 14.29 |
| PD | 0 | 0 |
| CR+PR | 6 | 85.71 |

| Bset Response | N (7) | % |
|---|---|---|
| CR | 1 | 14.29 |
| PR | 3 | 42.86 |
| SD | 1 | 14.29 |
| PD | 2 | 28.56 |
| CR+PR | 4 | 57.15 |

## Pathological response ( N=7 )




| Bset Response | N (7) | % |
|---|---|---|
| pCR | 4 | 57.15 |
| MPR | 2 | 28.58 |
| pCR+MPR | 6 | 85.71 |

| Bset Response | N (7) | % |
|---|---|---|
| pCR | 1 | 14.29 |
| MPR | 1 | 14.29 |
| pCR+MPR | 2 | 28.58 |

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