INTRODUCTION

Murlentamab (GM102)

Murlentamab is a glyco-engineered monomonal humanized IgG1 antibody displaying high affinity towards both:

- AMHRI, the receptor of Anti-Mullerian hormone of type II, present on tumor cells, via its Fab fragment
- CD16, present on effector cells, via its low affinity Fc fragment (Enabling technology platform)

Murlentamab restores tumor associated macrophages (TAM) anti-tumoral functions and NK engagement, resulting in enhanced tumor phagocytosis and cytotoxicity.

Macrophage shift from M0 to M1 phenotype

- Decreasing of CD206 and increase of immunosuppressive cytokines (IL-10, IL-4)
- Increase of pro-inflammatory cytokines and chemokines (CXCL9 and CXCL10)

AMHRI EXPRESSION IN SOLID TUMORS

Fixed tissues, IHC study:

- 907 samples analyzed
- AMHRI staining frequency and intensity similar to gynecological cancers in 4 other solid tumors

Fresh tissues, FACS study:

- 52 samples analyzed in CRC and ovarian cancer (OC)
- In CRC, AMHRI expression observed in 73% of samples:
  - mean 56,000 receptors per cell,
  - homogenous intratumoral distribution,
  - no expression in healthy margins

C201 STUDY DESIGN

MURLENTAMAB IN LOCAL ADVANCED OR METASTATIC COLORECTAL CANCER

Measurable disease

Having failed previous line of treatment

Performance status ≤ 2, adequate organ function

Resipalble lesion (2 lesions planned - baseline and under treatment)

COHORT I = murlentamab (7 mg/kg q4w)

15 evaluable patients

- Refractory patients (> 4 chemotherapies or ≥ 3 targeted therapies)

Pre-therapeutic

Under treatment

0
50
100
150
TGR cohort 1
TGR (%)
p-value = 0.0488

Studies

- Overall Response Rate (ORR) in each cohort
- Tumor Growth Rate (TGR)
- Clinical Benefit Rate (CBR), defined as CR+PR+SD
- Progression Free Survival (PFS)
- Pharmacodynamic evaluation (tumors and peripheral blood)
- Overall Survival (OS)
- Safety

STUDY ENDPOINTS AND STATUS

ENDPOINTS

Primary

- Overall Response Rate (ORR) in each cohort

Secondary

- Tumor Growth Rate (TGR)
- Clinical Benefit Rate (CBR), defined as CR+PR+SD
- Progression Free Survival (PFS)
- Pharmacodynamic evaluation (tumors and peripheral blood)
- Overall Survival (OS)
- Safety

SPECIAL

Murlentamab was very well tolerated with few toxicities

In total 36 murlentamab toxicities were reported in 30 patients in the combination cohort only

- All G1-G2
- Most common: decreased appetite (9 events), vomiting, nausea, constipation and asthenia (3 events each)

CONCLUSIONS

- This pilot study suggests longer than expected PFS for murlentamab + trifluridine/tipiracil in advanced mCRC, especially for patients with high AMHRI expression

- Immune activation of the macrophage / cytotoxic T cell cascade was observed in tumor microenvironment as well as in peripheral blood

- Murlentamab was very well tolerated with no overlapping toxicities with trifluridine/tipiracil

- These clinical results are encouraging for further development of murlentamab in combination with standard chemotherapies

- Translational research results open the field for exploring combination of murlentamab with other immunotherapy agents, especially targeting T cells