ONCOS-102 (Ad5/3-D24-GMCSF) is a tumor-targeted oncolytic adenovirus coding for human GM-CSF. Intratumoral ONCOS-102 induces a systemic CD8+ T cell response against patient’s unique cancer cells:

- **Recognition of threat**
  - Innate Immune System
- **T cell activation**
  - Adaptive Immune System
- **Immune attack**
  - Anti-tumor Immune Response

### Phase I study - design

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<th>Day</th>
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Dose cohorts: 3x10^8, 1x10^9, 3x10^10 viral particles

12 basal line patients with 100% chemorefractory solid tumors were treated at 3 dose levels (3+3+6 pts)

- **Strong co-stimulation**
  - Tumor
  - Lymph node

### Local GM-CSF expression

- Targeted anti-tumor immune response:
  - ONCOS-102 traffics immune system to recognize unique cancer cells of each patient
  - ONCOS-102 teaches immune system to recognize unique cancer cells of each patient
- Adaptive immune response:
  - In situ vaccination
  - Immunological memory
  - Provides long term protection

### Infiltration of innate and adaptive immune cells into tumors was seen following ONCOS-102 administration

- **Infiltration of innate**
  - Baseline
  - After ONCOS-102

### Heterogeneity in CD68+ macrophage density was seen in tumors before and after ONCOS-102 administration

- **CD68+ cells in tumors**
  - ONCOS-102
  - Before and after ONCOS-102

### CONCLUSIONS

- **High density of tumor infiltrating CD68+ macrophages at baseline was associated with short survival suggesting that these macrophages had tumor promoting phenotype**
- **ONCOS-102 -triggered CD68+ cell infiltration correlated with prolonged survival suggesting that these cells had different phenotype from CD68+ cells present in tumors before ONCOS-102 treatment**
- **Infiltration of multiple innate and adaptive immune cell populations after ONCOS-102 administration correlated with increased OS**
- **ONCOS-102 has potential to activate immunologically silent tumor and reduce the local immune suppression in advanced tumors**