A first assessment of CD8-PET/CT with 89-Zr-Crefmirlimab as predictive biomarker for response to standard of care immunotherapy in patients with solid tumors.

Guillaume Potdevin*, Isabelle Ayy, Laura Dillion, Emilie Mahieu, Hadassah Sade and Günter Schmidt

AstraZeneca Computational Pathology GmbH, Munich, Germany. *guillaume.potdevin@astrazeneca.com.

Parthenon Therapeutics, 40 Guest St, Boston, Massachusetts 02135, US

Background

- CD8-PET (immunoPET) is a novel imaging allowing for the in vivo visualization of the CD8+ cells population in humans.
- AZ engaged with ImaginAb (IAB), Takeda and Pfizer in a pre-clinical study to gain early access to IAB’s Ph2a clinical trial data and evaluate.
- Several aspects of CD8-PET are presented here including CD8-PET’s ability to predict patient response to Standard of Care (SOC) Immuno-Oncology Treatment (IOT).
- In parallel IAB’s technology is implemented in several AZ studies, allowing for an evaluation of the operative aspects of CD8-PET’s implementation in clinical trials.

Materials and methods

- ImaginAb’s Ph2a BOT study recruited patients with advanced solid metastatic tumour undergoing SOC-IOT with or without previous treatment and in combination or not with chemotherapy. Some patients also underwent corticosteroid treatments.

<table>
<thead>
<tr>
<th>Indication</th>
<th>N</th>
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<tr>
<td>NSCLC</td>
<td>9</td>
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<tr>
<td>RCC</td>
<td>15</td>
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<tr>
<td>Melanoma</td>
<td>11</td>
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<tr>
<td>Bladder, Gastric, Esophageal, Head &amp; neck</td>
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Setting:
- Advanced or Metastatic Solid Malignancies
- Multi-site
- Pre-treatment and On treatment imaging.

Treatments:
- Pembrolizumab / Nivolumab
- Atezolizumab
- Ipilimumab
- Bevacizumab
- Chemotherapy

Discussion

By utilizing both volume and CD8 infiltration changes measured from pre-and early on-treatment CD8-PET data, the developed algorithm can accurately predict a patient’s response to IOT (as depicted in Figure 3a). However, Figure 3b highlights that the predictive power of the algorithm is greatly dependent on the number of lesions analyzed, indicating that intra-patient heterogeneity plays a critical role in assessing an individual’s response to IOT. Figure 4 shows that both CD8 infiltration and volume changes are only indicative of long-term patient response (stratification is statistically not significant) but convey complementary information. In addition, the lesion-wise analysis presented in Figure 6 enables the discrimination between several phenotypes of lesion response to IOT. For instance, early responding lesions exhibit a volume increase, which is consistent with a significant increase in CD8+ cells in the tumor volume. One hypothesis is that lesions with delayed response would only differ in the speed of the influx of immune cells in the lesion. On the other hand, stable and progressive lesions exhibit both a decrease in CD8 infiltration even early in the treatment. Lesions with a response then relapse phenotype single out by their strong volume decrease, which makes the CD8 infiltration unreliable. But as highlighted by figure 4 (and consistently with IOT PR assessment) they are also typically present in patients with a high level of heterogeneity at the patient level, enabling an accurate prediction of the overall patient response.

Conclusion

This study CD8-PET can be used as an early biomarker of response to IOT. It also offers great promises as a tool to investigate the mechanism of action of IO treatment. These results, if confirmed by a larger cohort of patients data, could be the basis for future personalized patient treatment strategies.