Background

- Immunotherapy agents in combination with chemotherapy, have altered the course of metastatic triple-negative breast cancer (mTNBC), an aggressive subtype of breast cancer associated with improved outcomes and a favorable response to CPIs.
- Checkpoint inhibitor (CI) therapy in combination with chemotherapy has been shown to prolong survival in mTNBC patients with PD-L1 positive baseline status; however, CPI monotherapy is less effective with objective response rates (ORRs) as follows: PD-L1-positive patients: 5% to 24%1-3
- ≥2L patients: 6%3

PIVOT-02 STUDY SCHEMA

Preliminary results from the TNBC cohort of the Phase 1/2 PIVOT-02 study: Clinical activity of BEMPEG plus NIVO observed in metastatic TNBC:

- IRCCS, Candiolo, Italy; 6POO Szpital Specjalistyczny w Brzozowie, Brzozów, Poland; 7Instituto Oncologico Baselga at Hospital University Clinic, University of the Balearic Islands, Palma de Mallorca, Barcelona, Spain; 8Princess Margaret Cancer Centre, Toronto, Canada; 9GZA Ziekenhuizen Campus Sint-Augustinus, Antwerp, Belgium; *Nektar Therapeutics, San Francisco, CA, USA. 9The University of Texas MD Anderson Cancer Center, Houston, TX, USA.

- BEMPEGaldesleukin Preferential Signaling Through the IL-2 Receptor Pathway
- BEMPEGaldesleukin (BEMPEG; NKTR-214) is a CD122-preferential IL-2 pathway agonist that has shown to increase tumor-infiltrating lymphocytes (TILs), T cell diarysection and PD-1 expression1-4
- BEMPEG combined with the CPI nivolumab (NIVO) has been shown to convert baseline tumors from PD-L1 negative (v1%) to PD-L1 positive (v1%)5
- Low levels of baseline TILs10-12 and T cell-inflammation are predictive of a poor response to CPIs

Study Design

- PIVOT-02 is a multicenter, Phase 1/2 study evaluating BEMPEG plus NIVO that includes a cohort of patients with mTNBC
- PIVOT-02 recently reported preliminary clinical and safety data for melanoma1 and mUC2, demonstrating BEMPEG plus NIVO was well tolerated with promising clinical benefit. Here, we report the first BEMPEG plus NIVO findings in the mTNBC cohort (data cut-off, July 1, 2019).

PIVOT-02 STUDY SCHEMA

DOSE ESCALATION ACROSS A RANGE OF SOLID TUMORS

DOSE EXPANSION

Key mTNBC Patient Characteristics
- Measurable disease per RECIST v1.
- ECOG PS 0-1.
- TNBC patients with ≥ 2L disease as of July 1, 2019 were efficacy evaluable defined as patients with ≥ 2L mTNBC who were chemotherapy naive at the time of PIVOT-02 study entry
- ≥2L patients were defined as patients with 2 or more measurable metastatic sites with ≥ 10% or ≥ 3cm in either site

Baseline Patient Demographics and Disease Characteristics

- Baseline immunohistochemistry (IHC) analysis for PD-L1 was performed using 28-8 pharmDx (Dako) and defined as PD-L1 negative (<1% tumor cell expression) and PD-L1 positive (≥1% tumor cell expression)
- In addition to PD-L1 status, other predictive or prognostic clinical factors included assessed age, disease-free interval (DFI), LND, number and type of metastatic sites, and prior taxane
- Early responders were defined as first-line (1L) pts with a metastatic relapse within 12 months of last chemotherapy in early-stage setting
- Tumor assessments were performed at screening and every 6 weeks (± 7 days) by investigator and Independent Central Radiology (ICR)
- Safety and tolerability were assessed by adverse event (AE) analysis reported by CTCAE v4.03

Treatment-Related Adverse Events (TRAEs) at RP2D

- Treatment is ongoing and last tumor assessment, 3L pts (0 0)

Clinical Activity

- Best % Change from Baseline in Target Lesion Size, RP2D TNBC (Efficacy Evaluative Population N=38) Best % Change from Baseline in Target Lesion Size, RP2D TNBC (Efficacy Evaluative Population N=38)

- All patients had 1 or more prognostic features or negative predictive clinical factors for CPI benefit, including PD-L1 negative status

BEMPEGaldesleukin Clinical Activity

- In the IL-2 Receptor Pathway

- BEMPEGaldesleukin (BEMPEG; NKTR-214) is a CD122-preferential IL-2 pathway agonist that has shown to increase tumor-infiltrating lymphocytes (TILs), T cell diarysection and PD-1 expression1-4
- BEMPEG combined with the CPI nivolumab (NIVO) has been shown to convert baseline tumors from PD-L1 negative (v1%) to PD-L1 positive (v1%)5
- Low levels of baseline TILs10-12 and T cell-inflammation are predictive of a poor response to CPIs

Clinical Activity of BEMPEG plus NIVO Appears to Be Regardless of PD-L1 Status*

- Of the 5 responders:
  - 4 of 5 responders are ongoing treatment
  - 1 responder no longer on treatment achieved maximal clinical benefit and response is continuing at last follow-up
  - Efficacy by ICR is consistent with these response data

Conclusions

- Clinical activity and prolonged responses were observed in patients with mTNBC who were treated with BEMPEG plus NIVO – notably in pts with poor prognostic features or negative predictive clinical factors (LDH ≥ 8, if metastatic sites, prior taxane, early relapse) for CPI benefit, including those who were baseline PD-L1 negative
- BEMPEG plus NIVO was well tolerated, with a manageable safety profile
- These data support the future development of BEMPEG plus CPI; with chemotherapy in mTNBC pts who are baseline PD-L1 negative, have poor prognostic features, and are refractory to prior chemotherapy regimens
- This study (NCT02983493) and registrational studies in other solid tumor settings are ongoing

REFERENCES