A ctDNA-directed, multi-center phase II study of molecular response adaptive immuno-chemotherapy in patients with non-small cell lung cancer: Analysis of Stage 1 of CCTG BR.36

Valsamo Anagnostou1,2, Cheryl Ho3, Garth Nicholas4, Rosalyn Anne Juergens5, Adrian Sacher6, Andrea Fung7, Paul Wheatley-Price4, Scott A. Laurie4, Benjamin Levy7, Julie Brahmer1,2, Archana Balan1, Noushin Niknafs1, Egor Avrutin8, Liting Zhu8, Mark Sausen9, Penelope Bradbury6, Jill O'Donnell-Tormey10, Pierre Olivier Gaudreau8, Keyue Ding8 and Janet Dancey3

1The Sidney Kimmel Comprehensive Cancer Center, JHSM, Baltimore, MD, USA, 2The Bloomberg-Kimmel Institute for Cancer Immunotherapy, JHSM, Baltimore, MD, USA, 3BC Cancer - Vancouver Cancer Centre, Vancouver, British Columbia, Canada, 4Ottawa Hospital Research Institute, Ottawa, ON, Canada, 5Juravinski Cancer Centre at Hamilton Health Sciences, Hamilton, ON, Canada, 6University Health Network Princess Margaret Cancer Centre, Toronto, Ontario, Canada, 7Kingston Health Sciences Centre, Kingston, Ontario, Canada, 8Canadian Cancer Trials Group, Queen’s University, Kingston Ontario, Canada, 9Personal Genome Diagnostics (Labcorp), Baltimore, MD, USA, 10Cancer Research Institute, New York, NY, USA

Study Design and Endpoints

• BR.36 was designed to validate (stage 1) and implement (stage 2) ctDNA molecular response in precision immuno-oncology decision making
• Primary Endpoints: establish definition, timing and concordance of ctDNA molecular response with radiographic RECIST response
• Secondary Endpoints: time to molecular response, correlation with PFS, OS

Results

• Trial activation: Oct 17, 2019, closed to accrual: Apr 5, 2022
• 98% ever-smokers, 98% stage IV, 52% female, 76% AC, 96% PD-L1+
• 50 enrolled patients followed for a minimum of 12 weeks
• BOR by RECIST 32%, by iRECIST 36%
• 45 evaluable patients, 35 with detectable ctDNA
• Evaluable mR rate 43% (90% CI: 29-58%)
• BR.36 (stage1) met its primary endpoint for concordance between ctDNA molecular and RECIST radiographic response

Conclusions

BR.36 stage 1 established the definition, timing and concordance of ctDNA molecular response with radiographic response. These findings are incorporated in the randomized, ctDNA-interventional second stage of the trial, which utilizes ctDNA molecular response after 2 cycles of pembrolizumab to identify patients with mPD who are randomized to treatment intensification with pembrolizumab and chemotherapy.

Funded by the Cancer Research Institute and the Mark Foundation