A Phase III, Randomized, Placebo-Controlled Trial of Adjuvant Nivolumab Plus Ipilimumab in Patients (pts) With Localized Renal Cell Carcinoma (RCC)who Are at High Risk of Relapse After Radical or Partial Nephrectomy (CheckMate 914)

A. Bex[1], V. Grünwald[2], P. Russo[3], Y. Tomita[4], E. Berghorn[5], M..B. McHenry[6], R.J. Motzer[7]
Author Affiliations

- 1Department Of Urology, Netherlands Cancer Institute, 1066 CX - Amsterdam/NL
- 2Department Of Hematology, Hemostasis, Oncology, And Stem Cell Transplantation,, Hannover Medical School, 30625 - Hannover/DE
- 3Department Of Surgery, Memorial Sloan Kettering Cancer Center, 10065 - New York/US
- 4Department Of Molecular Oncology, Niigata University Graduate School of Medical and Dental Sciences, 951-8520 - Niigata/JP
- 5Global Clinical research, Bristol-Myers Squibb, 08540 - Princeton/US
- 6Global Biometeric Sciences, Bristol-Myers Squibb Company, NJ 08648 - Princeton/US
- 7Department Of Medicine, Memorial Sloan-Kettering Cancer Center, 10065 - New York/US

Background
Surgery is the standard treatment for non-metastatic RCC. Unfortunately, pts with stage II or III RCC have high risk of relapse with 5-year survival rates of 20% to 53%; prevention of recurrence is an unmet need. In CheckMate 214, the nivolumab + ipilimumab treatment combination demonstrated significant improvement in overall survival (OS) in first-line treatment of pts with advanced or metastatic RCC, with a manageable safety profile. This phase III multinational study will evaluate adjuvant nivolumab + ipilimumab vs placebo in pts with high risk of relapse after nephrectomy (NCT03138512).
Trial design
Key inclusion criteria: Radical or partial nephrectomy with negative surgical margins >4 weeks and ≤12 weeks before randomization; predominantly clear primary tumor cell histology; pathologic TNM staging T2a (grade [G] 3 or 4), T2b (any G), T3 (any G), or T4 (any G) N0M0, or any T (any G) N1M0; Eastern Cooperative Oncology Group performance status ≤1, no clinical/radiological evidence of macroscopic residual disease or distant metastases post-nephrectomy, and tumor tissue obtained ≤3 months pre-enrollment. Key exclusion criteria: Pts with conditions requiring corticosteroid or immunosuppressive systemic treatment, autoimmune disease, prior treatment with drugs specifically targeting T-cell co-stimulation or checkpoint pathways, and prior systemic treatment for RCC. Pts are randomized 1:1 to receive nivolumab and ipilimumab at the specified dose on specified days for 24 weeks, or placebo infusions on the same schedule for 24 weeks or until recurrence, unacceptable toxicity, or withdrawal of consent. Stratification factors: TNM staging and type of nephrectomy procedure. Primary endpoint: Disease-free survival per blinded independent central review. Secondary endpoints: OS, safety, and tolerability. Tertiary/exploratory endpoints include disease-related symptoms based on the Functional Assessment of Cancer Therapy-Kidney Symptom Index, and changes in global health status based on EuroQoL's EQ-5D-3L. Enrollment began July 2017 with a target of 800 pts.
Clinical trial identification
NCT03138512.
Legal entity responsible for the study
Bristol-Myers Squibb.
Funding

Bristol-Myers Squibb and Ono Pharmaceutical Company Limited.