Checkpoint blockade therapy

**IMMUNOTHERAPY TRIALS LACK A BIOMARKER FOR INCLUSION: IMPLICATIONS FOR DRUG DEVELOPMENT**

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**Background** Next-generation sequencing and other biomarkers have demonstrated the capability to identify potentially genomic molecular aberrancies. Immune checkpoint inhibitors (ICI) have benefited patients in almost every oncologic histologic. Combining these innovations has transformed how oncologists treat previously untreatable diseases.

**Methods** The 413 trials from clinicaltrials.gov website were reviewed using the terms ‘nivolumab’ or ‘pembrolizumab’ between January 1, 2019 and December 31, 2019. Additionally, all 33 interventional therapeutic trials for ‘glioblastoma multiforme’ and 79 for ‘pancreatic cancer’ that were either recruiting, not yet recruiting, or active not recruiting trials between January 1, 2019 and December 31, 2019 were analyzed.

**Results** In total of 413 trials, 57,853 were planned for enrollment with 37 (8.96%) trials requiring a biomarker for entry (n = 5,602 [9.7%]). Overall, there were 41 trials with single-agent immunotherapy planned to enroll 6222 patients and of those trials 7 (17.1%) required a biomarker for enrollment (n = 285 [4.6%]). There were 193 trials with >2 immunotherapies combined planned to enroll 21,360 patients and of those trials 7 (8.8%) required a biomarker for enrollment (n = 1254 [5.9%]). There were 69 trials with immunotherapy and chemotherapy combined planned to enroll 12,354 patients and of those trials 3 (4.3%) required a biomarker for enrollment (n = 83 [0.67%]). There were 58 trials with immunotherapy and targeted therapy combined planned to enroll 11,967 patients and of those trials 6 (10.3%) required a biomarker for enrollment (n = 3244 [27.1%]). There were 52 trials with other immunotherapy combinations (e.g. vaccine) planned to enroll 5950 patients and of those trials 4 (7.7%) required a biomarker for enrollment (736 [12.4%]). Within pancreatic cancer, 31 trials were planned to use immunotherapy (monotherapy, combination, with chemotherapy, with targeted therapy) including 4493 patients total; 5 (16%) of those trials required biomarkers enrolling 309 (7%) patients. Within glioblastoma multiforme, 13 trials were planned to use immunotherapy (monotherapy, combination, with chemotherapy, with targeted therapy) including 730 patients total; 7 (53%) of those trials required biomarkers enrolling 304 patients including 272 NSCLC, 24 UC and 8 RCC subjects were evaluated. 54 patients underwent a minimum of one PRBC transfusion during the pre-specified time period. Both median PFS (8.2 months versus 3.9) and overall survival (OS) were improved in the transfused population. N refers to non transfused population. Y refers to transfused population.

**Conclusions** For immunotherapy-based trials in 2019, <10% of patients expected to be enrolled would be selected by a biomarker for inclusion. Precision oncology continues to struggle in the era of ICI with an all-comers approach to patient selection and trial initiation. Selecting patients for trials based on biomarkers may help better identify responders to ICI.