Using RWD to provide natural history information

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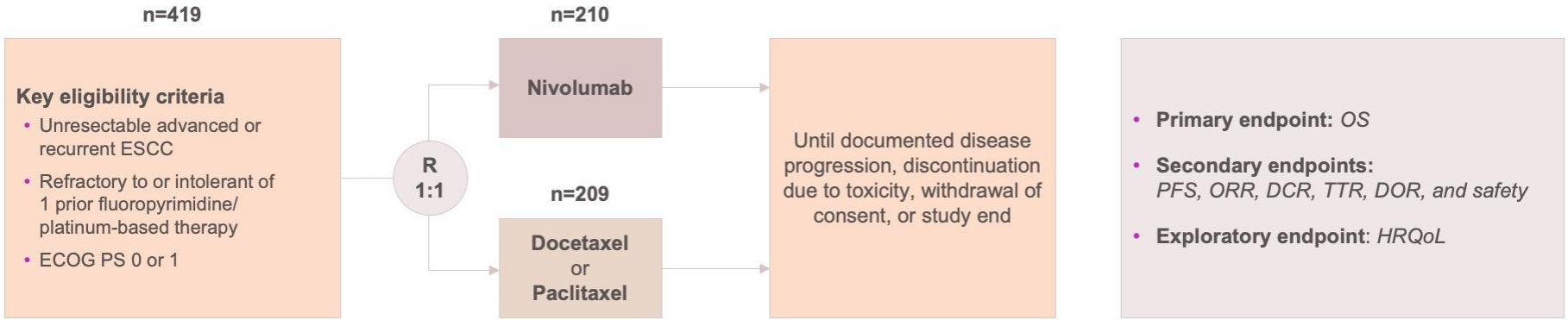
The need for RWD in Esophageal Squamous Cell Carcinoma

ATTRACTION-3 (ATT-3) was a global, multicenter, phase 3, randomized, open-label trial of nivolumab vs docetaxel or paclitaxel in patients with confirmed esophageal squamous cell carcinoma, refractory or intolerant to 1 prior fluoropyrimidine and platinum-based combination therapy



- **Second-line (2L) nivolumab therapy appeared to confer survival advantage compared with taxanes (10.9 vs 8.4 months) in ATT-3**
- **Patient enrollment occurred predominantly in Asia and hence regulatory concerns around applicability of ATT-3 to the US population (Western patients,18/419)**

Abbreviations: ATT *RWD: Real World Data; OS: Overall Survival; PFS: Progression Free Survival; ORR: Overall Response Rate; DCR: Disease Control Rate; TTR: Time to Response; DOR: Duration of Response; HRQoL: Health Related Quality of Life*

The need for RWD in Esophageal Squamous Cell Carcinoma

Evidence gaps

The prognosis of patients with unresectable, locally advanced or metastatic esophageal squamous cell carcinoma (adv/met ESCC) was poor in the USA

Outcomes of patients receiving 2L therapy for adv/met ESCC remained uninvestigated

Real world outcomes of second-line (2L) therapies as per NCCN treatment guidelines for adv/met ESCC was unexplored

Key research questions

What are the demographics, clinical characteristics and treatment patterns for patients with adv/met ESCC in the US?

What is the overall survival for adv/met ESCC patients who received at least two lines of therapy?

How different is survival among patients who received taxane 2L therapy and those who received non-taxane 2L therapy?

Leveraging RWD to support ATTRACTION-3 results

- BMS identified a cohort of real-world US patients receiving routine clinical management for adv/met ESCC using Flatiron database
- **86 adv/met ESCC patients** in the US receiving 2L treatment were identified during the period from 01/2011 – 01/2019
- In all patients who received 2L therapy median (95% CI) **OS from start of 2L was 6.7** (5.1–8.3) months. Median (95% CI) OS was **7.3 (5.9–11.5) months in patients who received 2L taxane-based therapy (n = 37)**
- Median OS observed in patients receiving taxane therapy in ATTRACTION-3 (8.4 months) was comparable to those in Flatiron database (7.3 months)

Outcomes	*ATTRACTION-3*[1]		*Flatiron Data*[2]	
Treatment arms	Nivolumab	Docetaxel or paclitaxel	All 2L patients	Taxane Therapies
Patients, *n*	210	209	86	37
Age (range), *years*	64 (57-69)	67 (57-72)	64 (36-83)	63 (36-81)
Male, *n (%)*	179 (85%)	185 (89%)	61 (70.9%)	29 (78.4)
Race, *n (%)*				
Asian	201 (96%)	200 (96%)	6 (7%)	2 (5.4%)
White	9 (4%)	9 (4%)	52 (60.5%)	22 (59.5%)
Median OS (95% CI), months	10.9 (9.2–13.13)	8.4 (7.2–9.9)	6.7 (5.1-8.3)	7.3 (5.9-11.5)
12-month survival (95% CI), %	47 (40–54)	34 (28–41)	28.4 (23-34)	29.3 (21-38)

Inclusion Criteria

Diagnosis of adv/met EC (index date), aged 18 years or older at index date, ≥ 1 month of medical data following and including index date, confirmed squamous or adenosquamous EC, received platinum and fluoropyrimidine based treatment as 1L for adv/met EC on or after the index date, received paclitaxel or docetaxel as 2L, ECOG score 0 or 1 any time after the index date

Exclusion criteria

Other primary cancers any time during the study period, with CT study medications on or after the index date, with autoimmune disease, interstitial lung disease or pulmonary fibrosis, diverticulitis or gastrointestinal ulcerative disease, brain metastases, pregnant, received paclitaxel or docetaxel before index date or nivolumab, pembrolizumab, durvalumab, atezolizumab, avelumab, ipilimumab, tremelimumab or immunotherapy any time during the study period

1. Kato K, et al. *Lancet Oncol* 2019;11:1506–17.
2. Abraham P, et al. *Adv Ther.* 2020;37:3392–403.

Impact of Real-World Evidence for BMS in Esophageal Squamous Cell Carcinoma

Key insights

Only **23-33% of patients treated in 1L received 2L therapy**. Survival among all patients receiving 2L therapy for adv/met ESCC was generally poor

Small proportion of patients receiving 2L therapy and poor survival highlighted the **unmet need for more effective therapies**

Clinical characteristics and outcomes **were comparable across regions in advanced stages of disease applicable to the US population and medical practice**

Impact

Inclusion of the Flatiron data along with other real-world analyses strengthened the BMS FDA filing to receive approval of this indication in June 2020.

Nivolumab was the first and only IO therapy approved for 2L ESCC regardless of PD-L1 expression in the US