This abstract was submitted to the DTRF Research Workshop in September, 2018.

TITLE: CAN WAIT AND SEE BE THE STANDARD OF CARE FOR INITIAL APPROACH TO PRIMARY SPORADIC DESMOID TUMORS? PRELIMINARY DATA FROM AN ITALIAN SARCOMA GROUP PROSPECTIVE STUDY.

AUTHORS (FIRST NAME, LAST NAME): Chiara Colombo1, Marco Fiore1, Giovanni Grignani2, Erica Palesandro2, Paola Boccone2, Lorenzo D’Ambrosio2, Alba Bianco1, Paola Collini1, Elena Palassini1, Silvia Stacchiotti1, Angelo Paolo Dei Tos3, Paolo Casali1, Federica Perrone1, Alessandro Gronchi1

INSTITUTIONS (ALL): 1. Fondazione IRCCS Istituto Tumori Milano, Milan, Italy. 2. IRCCS Istituto Candiolo, Torino, Italy. 3. Ospedale di Treviso, Treviso, Italy.

ABSTRACT BODY:

Objective: In recent years, retrospective evidence of long term disease stabilization and spontaneous regression of sporadic desmoid tumor (SDT) has been provided. As a result, a frontline wait and see approach (W&S) has been more routinely proposed. CTNNB1 coding for β-catenin is mutated in more than 90% of patients. Furthermore, a specific mutation (45F) was found to be correlated with a worse post-surgical local outcome. However, the prognostic role of β-catenin mutations is not fully understood and has never been explored in patients under W&S before any active therapy is performed. The main objective of this study was to prospectively evaluate the role of W&S in patients with primary SDT and to correlate β-catenin mutational status with the clinical outcome.

Methods: This is a prospective, multicenter (Fondazione IRCCS Istituto Tumori Milano and IRCCS Istituto Candiolo) observational study (founded by Ministero della Salute, Ricerca Finalizzata- NCT 02547831), performed among Italian Sarcoma Group centers and aim at evaluating the progression rate in patients affected by primary SDT managed with a front-line conservative approach (W&S). Active treatments were only proposed upon clear disease progression. β-catenin mutational status has been analyzed. Inclusion criteria were:

- Pathological diagnosis of SDT
- Primary disease at diagnosis or incompletely resected residual disease (R2 resection)
- Intra- and extra-abdominal SDT
- Histological diagnosis confirmed by expert sarcoma pathologists (PC and MB) according to the WHO criteria
- Measurable disease evaluated by on contrast-enhanced MRI (ce-MRI) T1 and T2 weighted images or contrast enhanced CT scan (for intra-abdominal location) Patient and tumor-related factors, treatment variables, follow up findings, time to progression and status at last followup were recorded.

Follow-up (FU) schedule required clinical evaluation and ce-MRI (or CT scan) at 3, 6, 9, 12 months, then every 6 months until the third year. Upon progression, defined as tumor growth proven by imaging and/or clinical examination, active treatments were proposed according to physician’s preference and registered in the clinical database.

Results: Between 2013 and 2018 a total of 114 patients entered the study (82% female, 18% male); median age 39 (IQ, 35-49) years; sites distribution: abdominal wall (52%), trunk (24%), extremity (18%), intra-abdominal (3%), head/neck (3%). CTNNB1 mutational status was available in 87% of patients. Median follow-up was 11 (IQ, 6-23) months. At the time of last follow up: 4/114 had spontaneous
complete regression, 23/114 spontaneous partial regression, 36/114 stable disease, 48/114 progression. For the last 3 patients enrolled status is still unknown. Among patients with stable disease, 6/36 initially experienced a progression and 5/36 initially experienced partial regression, while disease remained stable after that. Among patients with progression, 34/48 needed to start an active treatment. The median time to an active treatment was 6 (IQ range, 4-13) months. A preliminary analysis on the correlation between β-catenin mutational status and outcome revealed that 6/11, 12/51, 4/20 and 5/18 patients with DT harboring 45F, 41A, WT or other mutations had to start an active treatment for progression, respectively. No patient required surgery after enrolment.

Conclusion: This study prospectively confirmed that W&S for primary SDT is safe in light of the high rate of regressions and spontaneous growth arrest. SDT have a favourable course in more than 50% of patients. A higher risk of worse outcome for patients harbouring 45F was observed on the initial analysis but needs further validation on a longer FU. Upon progression, active treatments were considered on an individualized basis, while persisting in the W&S could still pay off.