TITLE: DESMOID TUMOR AND MOLECULAR TESTING FROM PATIENT REPORTED DATA IN AN INTERNATIONAL NATURAL HISTORY STUDY

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OBJECTIVES: Desmoid tumors (DTs) are commonly associated with mutations in the *CTNNB1* gene (sporadic DTs) or the *APC* gene (Familial adenomatous polyposis (FAP)-related DTs). Although mutational testing is recommended to confirm diagnosis and guide treatment by a consensus of DT experts, it is not clear to what extent testing is performed. Patient reported data are described here for those participants who have reported receiving mutational testing.

METHODS: The web-based natural history study launched September 2017 in collaboration with the National Organization of Rare Disorders. It contains 15 surveys covering diagnostics, disease, treatment, care management, and quality of life. Independence testing was performed using Pearson's chi squared test.

RESULTS: Of the 696 participants that have consented and started surveys, 302 have completed the surveys pertaining to molecular testing. Ninety-five (31%) report mutational testing and 188 report not having had mutational testing (62%), Male participants tended to have had molecular testing more often than female participants (38% of male vs. 28% of female) but was not statistically significant. American Indian or Alaska Natives had the lowest rate of molecular testing (0/3). Seventy percent (7/10) of Black or African American participants did not have molecular testing, while 167/261 (64%) of White participants did not have molecular testing. Although not reaching statistical significance, this data suggests that molecular testing is low across all races but may be disproportionately lower in American Indian or Alaska Native and Black or African American populations. This may be attributed to an unbalanced race population in the study, along with access to testing. Chest wall and abdominal wall tumors were the least likely to have mutational testing performed (28% for each) while intra-abdominal tumors the most likely (43%). Molecular testing for intra-abdominal tumors may be higher than others because they are more commonly associated with FAP-related DTs. Misdiagnosis rates were similar across those with mutational testing and those without. It is not clear, however, if the mutation information assisted in the eventual DT diagnosis. Taken together, it does not appear that mutational testing is used heavily in diagnosis at this time.

Specific mutations of the *CTNNB1* have been identified in DTs (include 41A, 45F, and 45P mutations). In this data, 28 participants reported the status of the *CTNNB1* gene: five were wild-type and 23 had a mutation. The specific mutation did not correlate with recurrence or with response to surgery. However,

it appears that a mutation in the *CTNNB1* gene does increase recurrence as compared to wildtype and continued growth following surgery.

CONCLUSION: DTs are most common in women with a median incidence of 30-40 years. They are associated with mutations in the *CTNNB1* and *APC* genes but mutational testing is not often provided, although it is the current recommendation. Natural history studies are an important tool to assess this rare tumor population. American Indian or Alaska Native and Black or African Americans may receive fewer mutational testing than white participants. However, due to lack of diversity in the study population this difference is not statistically significant. Similarly, due to a small sample size, *CTNNB1* mutations may indicate poor response to surgery and increased recurrence, but more data is needed.

		Has the Participant had any genetic or molecular testing?		
		Yes	No	Unknown or No Response
Gender (n = 302)				
	Male	35 (38%)	49 (54%)	7 (8%)
	Female	58 (28%)	139 (67%)	12 (6%)
	Transexual	2 (100%)	0 (0%)	0 (0%)
Race (n = 302)				
	American Indian or Alaska Native	0 (0%)	3 (100%)	0 (0%)
	Asian	3 (75%)	0 (0%)	1 (25%)
	Black or African American	2 (20%)	7 (70%)	1 (10%)
	Other	2 (40%)	3 (60%)	0 (0%)
	Refused or No Response	4 (21%)	8 (42%)	7 (37%)
	White	84 (32%)	167 (64%)	10 (4%)
Misdiagnosed (n = 284)				
	Yes	40 (35%)	70 (61%)	4 (4%)
	No	52 (31%)	107 (64%)	7 (4%)
	Unknown or No Response	0 (0%)	2 (50%)	2 (50%)

Table 1. Demographics of participants who have responded to the molecular diagnostics questions. There are no significant differences between the sexes or races of those who have reported receiving molecular testing of their tumors. However, men and white participants tend to have higher rates of molecular testing. Additionally, there are no significant differences in the participants who reported being misdiagnosed initially to those who received a correct diagnosis.