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A Pilot Study Evaluating the Use of Sirolimus in Children and Young Adults with Desmoid-type Fibromatosis

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Deregulation of the mTOR pathway may play an important role in tumor biology when the APC/ β -catenin pathway is disrupted in desmoid-type fibromatosis (DT). A Desmoid Tumor Research Foundation grant-funded pilot study was conducted to determine whether sirolimus can block the mTOR pathway (primary aim) as well as determine whether it can safely be given in the pre-operative setting, decrease tumor size/recurrence, and decrease tumor-associated pain in children and young adults (secondary aims) with DT. Nine subjects ages 5 to 28 years were enrolled from 2014 to 2017 across 4 centers. Patient demographics and disease characteristics are summarized in Table 1. Sirolimus was feasible and was associated with a non-statistically significant decrease in pS706K activation (Figure 1).

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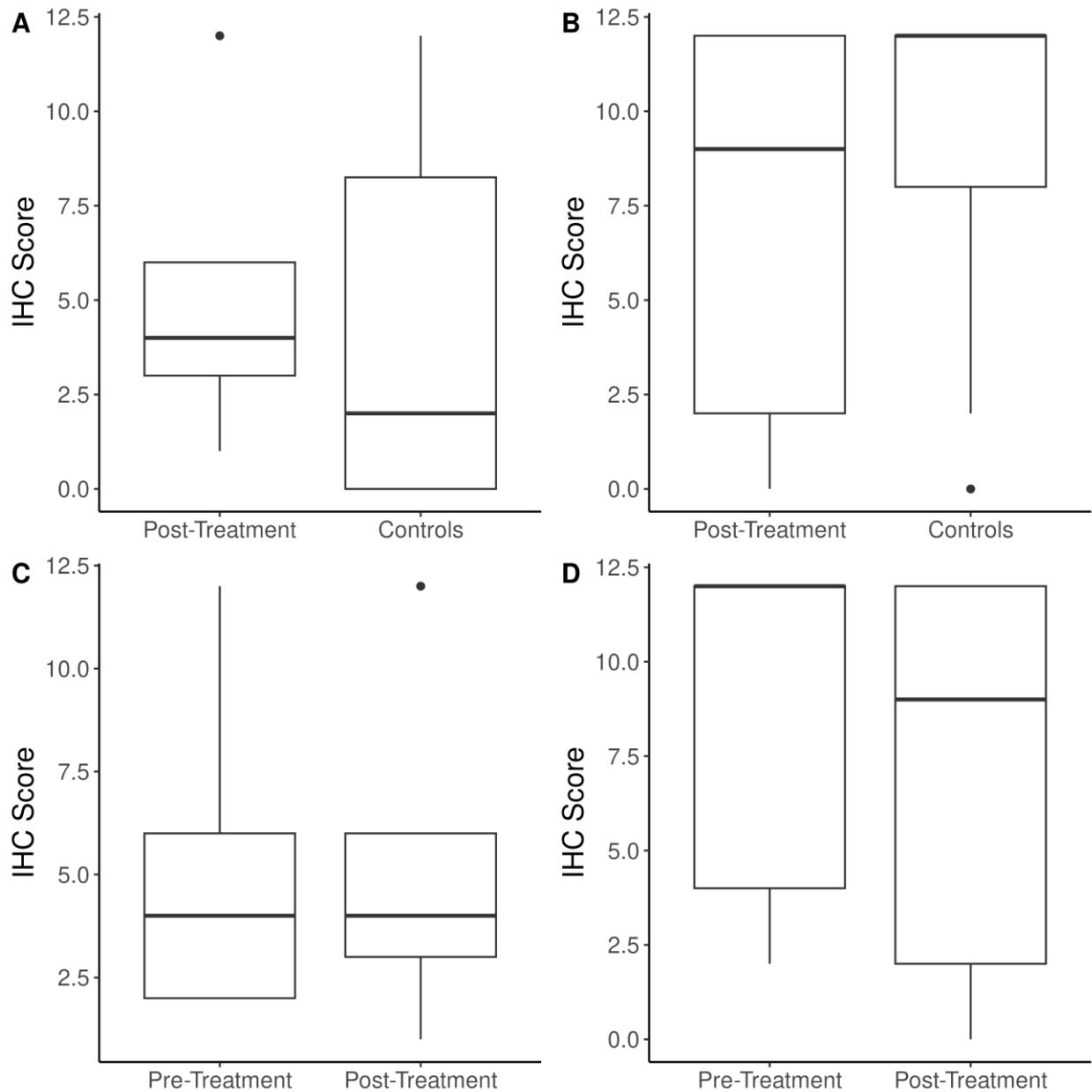
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†Deceased

TABLE 1 Patient demographics and disease characteristics

Characteristic	n (%)
Age (years)	
Median (range)	15 (5-28)
Sex	
M	6 (67%)
F	3 (33%)
Disease Status at Enrollment	
New Disease	2 (22%)
Progression/Recurrence	7 (78%)
Primary Site	
Head/Neck	1
Trunk	4
Extremity	2
Other	2
Presurgical Imaging Response	
Complete Response	0
Minor/Partial Response	0
Stable Disease	8
Progressive Disease	1
Surgical Outcome following Sirolimus	
Complete Resection	1
Microscopic Residual Tumor	4
Subtotal Resection	4

FIGURE 1 Boxplot of IHC scores for p4E-BP1 (A) and pS706K (B) in post-treatment trial patients versus control DT samples and for p4E-BP1 (C) and pS706K (D) in paired, pre-treatment versus post-treatment patients.*



*Bold line represents the median, box represents Q1 and Q3, tails represent min and max within 1.5*IQR, dots represent outliers. The average p4EBP IRS Score was 0.75 points higher (95% CI = -2.54, 4.04; $p = 0.63$) and the average pS706K IRS Score was 1.95 points lower (95% CI = -6.08, 2.19; $p=0.31$) in the post-treatment trial group compared to the control DT samples (Figures 1A and B). The average p4EBP IRS Score was 0.11 points higher (95% CI = -4.31, 4.09; $p = 0.95$) and the average pS706K IRS Score was 1.5 points lower (95% CI = -2.62, 5.73, $p=0.41$) after treatment with sirolimus compared to pre-treatment (Figure 1C and D) in paired patient specimens.