

DIETARY FIBER INTAKE IS ASSOCIATED WITH INCREASED TERTIARY LYMPHOID STRUCTURES IN DEDIFFERENTIATED LIPOSARCOMA FOLLOWING IMMUNE CHECKPOINT BLOCKADE

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Background Recent evidence suggests that dietary fiber intake is associated with improved clinical and pathologic response to anti-PD-1 therapy,¹ though this relationship is unclear in soft-tissue sarcoma. We evaluated the impact of dietary fiber intake on survival and the immune microenvironment in patients with surgically resectable dedifferentiated liposarcoma (DDLPS) and extremity/truncal undifferentiated pleomorphic sarcomas (UPS) treated with neoadjuvant immune checkpoint blockade (ICB) (NCT03307616).²

Methods Adult patients with treatment-naïve or locally recurrent resectable retroperitoneal DDLPS (n=17) or UPS (n=10) were randomized to receive either neoadjuvant nivolumab or nivolumab/ipilimumab, with UPS patients receiving concurrent radiation. Fecal and tumor samples were collected at baseline, after 1 cycle of ICB, and at surgery; dietary habits (NCI Dietary Screener Questionnaire [NCI-DSQ]) were collected at baseline. Fiber intake was derived from responses to the NCI-DSQ. Tumor infiltration by immune cells was assessed by multiplex immunofluorescence and presence of tertiary lymphoid structures (TLS) was assessed by immunohistochemistry of CD20 and CD21. Fecal microbiomes were profiled via metagenomic sequencing, MetaPhlan 3 and differential abundance analysis was performed using Analysis of Compositions of Microbiomes with Bias Correction (ANCOM-BC).³ Log-rank tests were used to compare survival curves. Wilcoxon rank sum tests were used to compare continuous variables between groups.

Results Median fiber intake was 16 g/day (IQR 13.6-18.4) and similar between the two histologic subtypes (p=0.27). Patients who consumed more (≥ 16 g/day) fiber had significantly improved overall survival when compared to patients who consumed less (p=0.025, Figure 1). Dietary fiber intake was significantly greater in DDLPS patients with a higher density of intratumoral cytotoxic T cells (CD3+CD8+/CD3+) at baseline (p=0.0088, Figure 2a). The presence of TLS at surgery was significantly associated with improved overall survival in DDLPS patients (p=0.031, Figure 2b), and fiber intake was significantly greater in patients with intratumoral TLS following ICB (p=0.0012, Figure 2c). Fiber intake was significantly higher in DDLPS patients who either gained or retained the TLS signature over their treatment course (p=0.0047). Multiple Firmicutes spp. were observed to be significantly associated with fiber intake and the presence of TLS at surgery (q<0.05) over the treatment duration.

Conclusions This study demonstrates that dietary fiber is associated with increased cytotoxic T cell infiltration and TLS formation in DDLPS treated with neoadjuvant ICB. Dietary fiber intake may represent a modifiable factor to improve response to ICB, and the stability of certain fecal microbial taxa may be clinically beneficial.

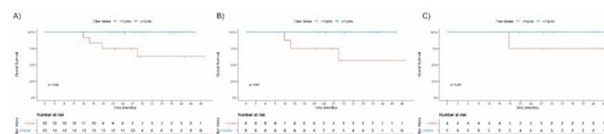
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Trial Registration ClinicalTrials.gov Identifier: NCT03307616

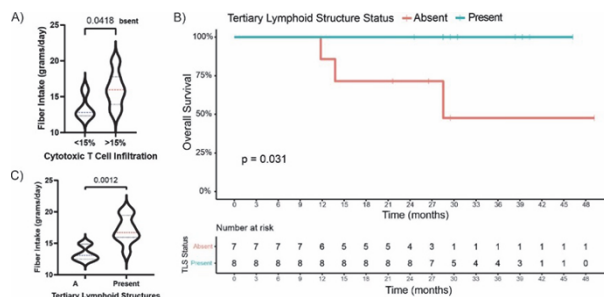
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Ethics Approval This study was approved by University of Texas MD Anderson Cancer Center's Ethics Board, approval number 2017-0143.



Abstract 618 Figure 1 Impact of dietary fiber on survival in resectable retroperitoneal dedifferentiated liposarcoma (DDLPS) and undifferentiated pleomorphic sarcomas (UPS). A) Kaplan-Meier curves of overall survival (OS) in DDLPS and UPS patients who had higher (≥ 16 g/day, n = 17) and lower (< 16 g/day, n = 8) fiber intake from date of first dose to death. B) Kaplan-Meier curves of OS in DDLPS patients who had higher (≥ 16 g/day, n = 8) and lower (< 16 g/day, n = 8) fiber intake from date of first dose to death. C) Kaplan-Meier curves of OS in UPS patients who had higher (≥ 16 g/day, n = 5) and lower (< 16 g/day, n = 4) fiber intake from date of first dose to death
Abbreviations: OS, overall survival; DDLPS, dedifferentiated liposarcoma; UPS, undifferentiated pleomorphic sarcoma



Abstract 618 Figure 2 Association of fiber with the immune microenvironment in retroperitoneal dedifferentiated liposarcoma. A) Fiber intake (g/day) of samples with higher ($> 15\%$) density of intratumoral cytotoxic T cells (n = 12) and lower ($< 15\%$) density of intratumoral cytotoxic T cells (n = 3) at baseline as assessed by multiplex immunofluorescence. B) Kaplan-Meier curves of OS in DDLPS patients who had TLS (n = 8) and those who did not have TLS (n = 7) at surgery from date of first dose to death. C) Fiber intake (g/day) of samples with TLS (n = 8) and those without TLS (n = 7) at surgery
Abbreviations: OS, overall survival; DDLPS, dedifferentiated liposarcoma; TLS, tertiary lymphoid structure.

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