Impact of Next Generation Sequencing (NGS) On The Treatment of Patients with Sarcoma

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Background and Objectives

- **Background:**
- NGS is increasingly being used for patients with Sarcoma
- The role of NGS in the management of patients with Sarcoma remains undefined
- Basket trials, and tissue agnostic therapies are increasingly prevalent and may be compelling options for patients in later lines of treatment
- **Objective:**
- To review usage of NGS testing in patients with Sarcoma
- To characterize the effect of NGS on management of patients with Sarcoma
- Better qualify instances in which NGS was utilized in order to understand incidence of mutations within a large population of Sarcoma patients

Methods

- Conducted through the Northwestern Medicine Oncoset Database
- Retrospectively analyzed all patients seen through the Northwestern Healthcare system with NGS, and a tissue diagnosis of Sarcoma
- Clinical course interpreted by investigators to assess impact on treatment and decision-making
- Mutations cross-referenced with ongoing tissue agnostic, and sarcoma specific trials
- **Key Eligibility Criteria**
  - Histologically confirmed diagnosis of Sarcoma
  - Performance of NGS assay:
    - Foundation Medicine
    - Tempus CDx
    - Guardant 360
  - Age > 16 years

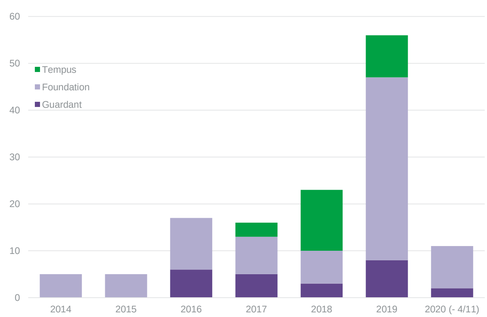
Results

- A Total of 117 patients were analyzed with assays performed between 2014 and 2020

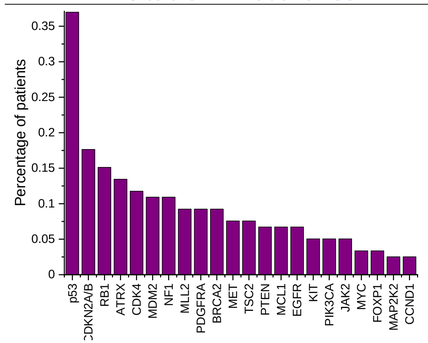
Patient Demographics and Clinical Characteristics

Characteristics	Frequency (%)
Age- Median (Range)	55 (20-94)
Male	57 (48%)
Female	60 (52%)
Assays Per Patient (Range)	1 (1-4)
Histologic Subtypes	
Leiomyosarcoma	36 (31%)
STS NOS	21 (18%)
Angiosarcoma	13 (11%)
Liposarcoma	11 (9%)
Other	36 (31%)
No Variants Detected	
Guardant	6 (25%)
Tempus	1 (2%)

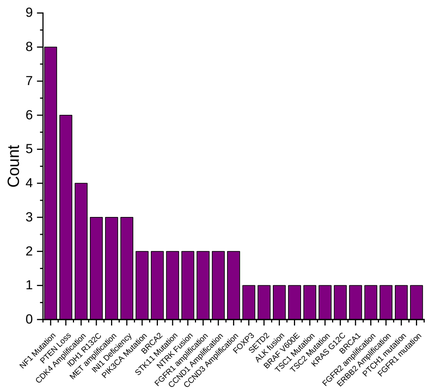
Assay Utilization Over Time



Mutation Prevalence



Actionable Mutations



Patients for whom NGS Altered Management

Histology	Mutation	Treatment
Ewings Sarcoma	PTEN Loss	Copanlisib
Leiomyosarcoma	ALK Fusion	Alectinib
Leiomyosarcoma	MSI-H	Nivolumab
Chondrosarcoma	IDH1	Ivosidenib
Synovial Sarcoma	BRAF V600E	Encorafenib
STS NOS	CDK4 Amplification	Palbociclib
STS NOS	CCND1 Amplification	Palbociclib
STS NOS	NTRK Fusion	Larotrectinib
Myxofibrosarcoma	High TMB	Atezolizumab

Notable Cases

- Myxofibrosarcoma with TMB of 888
- Leiomyosarcoma that is MSI-H
- Intimal Sarcoma with NTRK3 Fusion

Conclusions

- 34% of patients had potentially actionable Mutations
- Treatment of 8% of patients was altered by NGS results
- Incidence of actionable mutations increased over time
- Partial responses in select, refractory patients

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