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

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 quality 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%)

- **Mutation Prevalence**

- **Actionable Mutations**

- **Assay Utilization Over Time**

- **Patients for whom NGS Altered Management**
  - Ewings Sarcoma
  - Leiomyosarcoma
  - Leiomyosarcoma
  - Chondrosarcoma
  - Synovial Sarcoma
  - STS NOS
  - STS NOS
  - STS NOS
  - Myxofibrosarcoma

- **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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**Legend:**

- PTEN Loss
- ALK Fusion
- MSI-H
- CDK4 Amplification
- IDH1
- Encorafenib
- BRAF V600E
- Palbociclib
- CCND1 Amplification
- NTRK Fusion
- Atezolizumab

**Graphs:**

- Impact of Next Generation Sequencing (NGS) On The Treatment of Patients with Sarcoma
- Mutation Prevalence
- Actionable Mutations
- Assay Utilization Over Time

**Tables:**

- Potentially Actionable Mutations
- Percentage of patients

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**Histology**

- Ewings Sarcoma
- Leiomyosarcoma
- Synovial Sarcoma
- STS NOS
- Myxofibrosarcoma

**Mutation**

- PTEN Loss
- ALK Fusion
- MSI-H
- CDK4 Amplification
- IDH1
- BRAF V600E
- CCND1 Amplification
- NTRK Fusion
- High TMB

**Treatment**

- Copanlisib
- Alectinib
- Nivolumab
- Encorafenib
- Palbociclib
- Tarrectinib
- Atezolizumab