Utilization of Next Generation Sequencing in NET/NEC management and practice patterns: A Prospective Survey of Global NET Specialists

Chauhan A[A], Munir A[B], Hernando J[C], Leeuwaarde R V[D], Zhang P [E], Capdevila J [C], Bergsland E [F]

[A]University of Kentucky, Lexington, United States, [B]Sheffield Teaching Hospitals NHS, Sheffield, UK, [C]Vall d´Hebron University Hospital, Barcelona, Spain, [D]University Medical Center of Utrecht, Utrecht, Netherland, [E]Peking University Cancer, Beijing, China, [F]University of California San Francisco, San Francisco, USA

Background:

- Next generation sequencing (NGS) based somatic tumor mutation as well as germline mutation data is being increasingly used in cancer management.
- Pan tumor type FDA approval for NTRK fusion, intermediated-high tumor mutation burden and MSI high status has paved the way for tissue agnostic molecularly targeted therapies.
- Utilization of NGS in neuroendocrine tumor (NET) and neuroendocrine carcinoma (NEC) is currently unknown.

Aim:

To understand current practice patterns of NET/NEC specialist with regards to utilization of molecular testing for somatic and germline mutations in neuroendocrine neoplasms (NEN).

Methods:

- This is a 49 question, prospective, online, survey-based study
- 16 members of NET-CONNECT (https://net-connect.info/meet-the-experts/) from across European Union (Netherlands, Spain, Italy, Germany, France, Sweden), UK, Israel, USA and China participated in the study.
- Study is IRB approved and de-identified data is stored at University of Kentucky servers.

Demographics:

- 16 of total 23 NETCONNECT members completed the survey.
- 12 (75%) participants were from academic institutions.
- Top three specialties participating in survey were; 50% medical oncologist (GI), 31% endocrinologist and 6% thoracic oncologist.
- About 70% participants have been practicing for less than 10 years and remaining 30% over 10 years post completion of training.
- 93% participants reported their practicing facility to be a NET/NEC referral center.
- 37% specialists reported to see over 12 new NET patients per month whereas about 18% see 9-12 and another 18% see 5-8 new NET patients per month.

Conclusions

Role of NGS is evolving in NET/NEC. Our study highlights current practice patterns globally. Therapeutic implications of NGS testing seem to be relatively low for NEN at present but this could certainly change as and when more targeted therapies are available. We anticipate that incorporation of molecular fingerprinting in pathological classification of NENs will lead to wider utilization of NGS.

Author Contact Information: amanchauhan@uky.edu

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Results:

NGS (somatic) utilization in NET: 0% every time, 62.5% sometime to frequent and 37.5% never or rarely. Majority (59%) reported that they prefer to do NGS at the time of disease progression while about 22% orders NGS at the time of diagnosis of metastatic disease in NET cohort.

NGS (somatic) utilization in NEC: 6% every time, 56% sometime to frequent and 37 %never to rarely. Majority (46%) reported that they prefer to do NGS at time of diagnosis while 37.5% orders NGS at time of disease progression in NEC cohort.

NGS (germline) utilization in NEC vs NET: 67% participants reported to "never or rarely" utilize germline testing in NEC as compared to 31.25 % in NET. Commonest NETs to be tested for germline mutations were Para/Pheo at 27.27 % followed by pancreatic NET and Medullary Thyroid cancer at 22.73% each. 64% respondents reported that they refer patient to genetic counselor for germline mutation testing. Majority (75%) reported that there is lack of formal institutional policy for guidance regarding germline testing at their practice.

Other key findings:
Commonest NEN subgroups tested for somatic mutations are NEC at 27 % followed by non-pancreatic grade 3 NET at 22.92% and pancreatic grade 3 NET at 27%.

75% respondents reported that they have a dedicated molecular tumor board at their institution.

Commonest reported reasons for ordering NGS in NENs were molecular characterization/pathology (36%), clinical trial screening 33% and routine clinical care/off label therapies (27%)

62% respondents reported that they never/rarely incurred insurance issues for ordering NGS.

While most (80%) respondent reported receiving NGS results within 3 weeks, however about 20% did report a turnaround time of over 3 weeks.

73% respondents perceive value in ordering NGS however 90% respondents admitted that likelihood of patients receiving treatment based on NGS is less than 10%. This could imply that most people order NGS for molecular characterization of NETs rather than for its therapeutic potential. This notion is confirmed by the observation that 72% respondents reported using TP-53/Rb-1 status to differentiated NET vs NEC.

80 % respondents perceive value in ordering NGS for NEC patients. Although 75% respondents admit that only less than 10% patients qualify for targeted therapies based on NGS, however in contrast to NET cohort, 25% respondents believe that NGS can affect therapeutic choices in NEC. This is perhaps due to higher rate of mutations and potential targetable genomic alterations seen in NEC as compared to NET.

About 87 % respondents reported that they never or rarely order liquid biopsies (blood based NGS testing) for management of NET or NEC

Lastly the top four barrier for ordering NGS in NETs are as follows; lack of data (21.62%), concern that the results won't be actionable (21.62%), lack of consensus guidelines (18.92%) and inadequate tissue (16.22%)