Newer drugs in GIST – Global access issues

Dr Sameer Rastogi
Additional Professor, Sarcoma and GIST clinic
Dept of Medical Oncology
AIIMS, New Delhi
Email – samdoc_mamc@yahoo.com
Outline of talk

• Our experience with Avapritinib and Ripretinib

• Why global Easy access is necessary --The same was not the case with imatinib, sunitinib and regorafenib !

• Can something be done?
Avapritinib in advanced gastrointestinal stromal tumor: case series of the literature from a tertiary care center in India

• Starting dose was 300mg per day
<table>
<thead>
<tr>
<th>Primary site of tumor</th>
<th>Age (years)/sex</th>
<th>Mutation</th>
</tr>
</thead>
<tbody>
<tr>
<td>A Jejunum</td>
<td>28/male</td>
<td>c-KIT exon</td>
</tr>
<tr>
<td>B Duodenum</td>
<td>49/male</td>
<td>c-KIT exon</td>
</tr>
<tr>
<td>C Stomach</td>
<td>40/male</td>
<td>c-KIT exon</td>
</tr>
<tr>
<td>Dose</td>
<td>Response</td>
<td></td>
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</tr>
<tr>
<td>A 300 mg</td>
<td>Initial SD at 3 months followed by PD at 6 months</td>
<td></td>
</tr>
<tr>
<td>B 300 mg</td>
<td>Initial PR at 2 months, SD at 5 months followed by PD at 8 months</td>
<td></td>
</tr>
<tr>
<td>C 300 mg</td>
<td>PD</td>
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Rastogi S et el. FSOA 2021
PDGFRA D842V mutation pre and post imatinib

Rastogi S et al. FSOA 2021
Fig 1a – maximum intensity projection image of FDG PET-CT showing no Abnormal FDG uptake in the body Fig 1b represents axial CT showing non FDG avid hypodense lesions in liver (fig 1c)  
Fig 2a - maximum intensity projection image of FDG PET-CT showing no Abnormal FDG uptake in the body Fig 2b represents axial CT showing non FDG avid hypodense lesions in liver (fig 2c) – findings suggestive of complete response to therapy.

Post 1 year of avapritinib
Figure 3. Subdural haemorrhage in case 2. Computed tomography head of patient B showing biconcave hyperdensity in the right parieto-occipital location with associated midline shift suggestive of subdural hemorrhage.
Ripretinib

• So far 2 cases

• Unpublished

• Post avapritinib in both cases
<table>
<thead>
<tr>
<th></th>
<th>Primary site of tumor</th>
<th>Age (years)/sex</th>
<th>Mutation</th>
<th>Response to imatinib</th>
<th>Response to sunitinib</th>
<th>Response to regorafenib</th>
<th>Other treatments tried</th>
<th>Sites of metastasis</th>
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</thead>
<tbody>
<tr>
<td>A</td>
<td>Jejunum</td>
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<td>c-KIT exon 17</td>
<td>PR</td>
<td>PD</td>
<td>PD</td>
<td>Progressed on immunotherapy</td>
<td>Liver, omental, serosa</td>
</tr>
<tr>
<td>B</td>
<td>Duodenum</td>
<td>49/male</td>
<td>c-KIT exon 11</td>
<td>PR</td>
<td>PD</td>
<td>PD</td>
<td>Progressed on immunotherapy</td>
<td>Liver, omental, serosa, bone, nodes</td>
</tr>
</tbody>
</table>
1a – Maximum intensity projection (MIP) image of FDG PET-CT showing increased tracer uptake in the abdomen corresponding to nodule measuring 2.1x1.6cm in the greater omentum on CT (1b) showing increased FDG uptake on fused PET-CT (1c).

1d – Multiple lesions in both lobes of liver with increased FDG Uptake on fused PET-CT (1e).
2a – Maximum intensity projection (MIP) image of follow-up FDG PET-CT showing increased tracer uptake in the abdomen corresponding to multiple lesions in both lobes of liver (2d) with FDG uptake on fused PET-CT (decreased to previous scan 2e).

2b – Previously seen FDG avid omental nodule is not seen on follow-up CT abdomen (2b) with no FDG uptake (2c). Findings are suggestive of Partial response.
Case B
1A – Maximum intensity projection image of FDG PET-CT showing multiple areas of tracer uptake in the neck, abdomen and right thigh region corresponding to multiple liver lesions (1B), retroperitoneal lymph nodes (1D) and D1 vertebral lesion (1F, white arrows) on axial CT respectively showing FDG uptake on fused PET-CT images (1C, 1E and 1G) respectively.
2A – Maximum intensity projection image of FDG PET-CT showing multiple areas of faint tracer uptake in the neck and abdomen corresponding to multiple liver lesions (2B), retroperitoneal lymph nodes (2D), white arrows and D1 vertebral lesion (1F) on axial CT respectively showing FDG uptake on fused PET-CT images (2C, 2E and 2G) respectively. As compared to previous scan there is significant decrease in size and FDG uptake in the pathologic liver, D1 vertebral lesions and retroperitoneal lymph nodes.
Covid lesson – Inequality
The hardest thing to explain is the glaringly evident which everybody had decided not to see.

Ayn Rand
Russian-American novelist
(1905-1982)
Is compassionate basis program the real answer?

• Thanks to compassionate basis program but what are the downside of compassionate basis

• 1. Takes time
• 2. Needs educated patients who can do paper work in English
• 3. Sometimes might be erratic because of various reasons specially in COVID times
• 4. Only in expert centers
• 5. Mostly for local patients
How lack of clinical trials and poor access affects practice in GIST?

• Apathy amongst physicians

• Frustration amongst patients
How it affects practice in GIST

• Why should we do mutation testing if we don’t have advanced drugs

• People end up taking costly drugs like nilotinib, dasatinib, nivolumab

• Desired outcomes not obtained if appropriate drugs not prescribed for specific mutations
Possible Issues

At a policy level:

• Fragmented procuring systems
• Less priority on obtaining of drugs targeting rarer diseases/ lack of clinical trials in various countries.

At practitioners’ level:

• Lack of awareness on patient assistance programs
• Less confidence on use of newer drugs/side effect management due to lack of experience
How Access to Novel Drugs Impacts Treatment

Better access to novel drugs:
- Better decision making towards treatment
- Better quality of care administered
- Improves the disease outcomes

Lessons to learn: Availability of better targeted therapies e.g. Osimertinib is revolutionizing management of lung cancers in India, increasing survival
The Way Forward For Better Care

Multi-pronged approach toward improvement at levels of:

• Administrative
• Pharmaceutical
• NGOs and social organizations
• International medical associations and support groups
• The clinicians’ initiative