2nd Annual

RAS-Targeted Drug Development

Finally Bring an End to RAS Driven Cancer

September 14-16, 2020 | Digital Event

Speaker Interview

AN EXCLUSIVE INTERVIEW WITH:

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What is the biggest roadblock preventing a successful RAS therapeutic advancing to in-human trials?

Historically, RAS has been deemed as an undruggable target. Direct RAS inhibitors were not developed until the recent breakthrough of KRAS G12C irreversible inhibitors showed promises in the clinic. The attempts to tackle this pathway via targeting the upstream regulators or downstream effectors often failed due to lack of specificity or feedback upregulation of the pathway avoiding effective inhibition of the signaling. The advancement of KRASG12C-selective inhibitors to early clinical promise suggest that direct targeting of KRAS mutant is achievable in certain mutation context.

What is on the horizon for RAS Targeted Therapeutics?

On direct targeting RAS proteins, we are seeing efforts on KRAS G12D and G12V. Small molecule inhibitors are being discovered and optimized and hopefully will move into clinic soon. In addition to small molecule inhibition, the community is also testing other modalities including antisense oligonucleotide that targets the KRAS gene irrespective of its mutation status. Autologous T cells specific for mutant KRAS such as KRAS G12D have also been tested to target KRAS mu cancers. There are also more attempts of combination approaches to tarte the upstream regulators or downstream effectors. Among these, MEK, ERK, CRAF, SHP2 and EGFR are all important players. Various combinations of inhibitors of these targets and sometimes also include the KRAS G12C inhibitors may lead to more lasting pathway inhibitions.

It appears the industry is shifting focus toward a combination therapy approach. What do you believe to be the benefits and/or caveats to progressing this way?

Combination approach has its advantage in that it can address the feedback activation occurred after inhibition of single node of the RAS-RAF-MEK pathway. In that incidence, inhibition of multiple nodes of the pathway can lead to more sustained inhibition and potentially translate into more durable responses. In addition, multi-targeting approach may help to slow down the resistance development by cancer cells as the inhibitory pressure on different part of the cancer cell signaling may slow down its adaptive resistance development. Another critical point to take note for targeting RAS mutant cancers is the high heterogeneity within KRAS-mutant tumors. In order to address this issue, a combination approach by a multi-pronged targeting will have better therapeutic effect than single agent approach.

What are you most excited for at the 2nd RAS Targeted Drug Development summit?

This is an exciting forum for the community to come together and share our progress and learnings during our journey fighting RAS mutant cancers. It provides invaluable opportunities for people to share ideas and form collaborations.

What are your burning questions you want to ask our speakers/audience at the summit?

- What are your favorite approaches in targeting RAS mutant cancers?
- What do you think will be the most effective way to address resistance to the KRAS G12C inhibitors emerging in the clinic?
- How do you see targeted + I/O combination in targeting RAS mutant cancers?

A huge thank you to Lusong Luo for taking the time to speak to us and share his insights and excitements for the future of RAS targeted therapeutics.

Don't miss Lusong's presentation on day 2 of the RAS Targeted Drug Development Summit where he will be discussing the exploration of synergistic effects.

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