Terapias dirigidas (III)
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Poziotinib overcomes de novo resistance of HER2 exon 20 mutations in NSCLC and other cancers: Preclinical studies and initial clinical testing J. P. Robichaux

- POZIOTINIB es un inhibidor con actividad en Inserciones del exon 20 de EGFR (73% RR. Elamin et al IASLC 2017)
- HER2 está mutado en el 2% de NSLC la mayoría por inserciones en el exon 20
- POZIOTINIB inhibe in vitro e in vivo las inserciones de HER2 en exon 20
- Basados en estos datos preclínicos y en los resultados del estudio previo en inserciones del 20 de EGFR actualmente hay 2 estudios fase I de poziotinib en inserciones del 20 en EGFR y HER2 y otro estudio basket para otros tumores
4788 / 17 - Preclinical evaluation of E-191, a highly selective EGFR T790M inhibitor. L. Xile

- E-191 as a novel irreversible inhibitor that shown in vitro and in vivo a selective inhibitor of the resistance mutant forms of EGFR, potently inhibiting EGFR T790M but not EGFRWT.

- These results make us believe that E-191 has a good potential in the clinic for the treatment of resistant EGFR driven NSCLC.


- DBPR112 a potent EGFR-TKI showing excellent inhibitory ability on EGFRL858R/T790M and EGFR exon 20 insertion.

- DBPR112 was orally effective against the growth of human lung H1975 tumors subcutaneously xenografted in nude mice showing dramatic reduction in tumor size.

- DBPR112 was approved by US FDA in 2016 and the Phase I clinical trial has been initiated since July 2017 in Taiwan.
Nuevos inhibidores de EGFR de 3ª generación

4790 / 19 - YH25448, an irreversible 3rd generation EGFR TKI, exhibits superior anticancer effects with potent brain BBB penetration in NSCLC. J. Yun

YH25448, a highly mutant-selective and irreversible 3rd generation EGFR TKI potently penetrating blood-brain barrier (BBB) penetration, targets both activating EGFR mutations Del19, L858R and T790M mutation while sparing wild type

Superior in vitro potency and selectivity over osimertinib

Superior in vivo efficacy over osimertinib in both (del19, L858R) and double (L858R/T790M) mutant xenograft models

Excellent BBB penetration and superior in vivo efficacy over osimertinib in a brain metastasis model

Lower skin toxicity over osimertinib

Phase I/II clinical trial in EGFR mutant NSCLC patients are underway (NCT03046992)
OMO-1 is a potent, highly selective, orally bioavailable, MET kinase inhibitor with a favorable preclinical toxicity profile, showing both monotherapy activity, against MET pathway-driven tumors, and EGFR TKI combination activity in acquired resistance models. M. Libouban

- Induced regression of large MET amplified EBC-1 SqNSCLC
- Combination treatments were well tolerated and improved EGFR targeted therapy. Although single agent OMO-1 had no effect on NSCLC HCC827 EGFR, combination with Erlotinib led to delayed onset of tumor recurrence.