Solid Tumor Drug Updates

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Disclosures

I have nothing to disclose.

Objectives

- Recognize newly-approved drugs used in solid tumor malignancies
- Describe the mechanism of action of newly-approved drugs used in solid tumor malignancies
- Appraise primary literature leading to FDA approval of new agents in solid tumors
- Distinguish the place in therapy for newly approved drugs used in solid tumor malignancies

Choose your own adventure!

Genitourinary | Breast + Gyn

Lung | Miscellaneous

Genitourinary

1. Relugolix (Orgovyz®) – advanced prostate cancer
2. Tivozanib (Fotivda®) – advanced Renal Cell Carcinoma (RCC)

Relugolix (Orgovyx®)

- Approved December 18, 2020
- Adults with advanced prostate cancer

Mechanism of Action	Oral Gonadotropin-releasing hormone (GnRH) receptor antagonist
Dosing	360 mg PO on Day 1, then 120 mg PO daily
PK/DDIs	• Major substrate of Pgp • Minor substrate of CYP3A4 and CYP2C8 • t ½ = 25 hours
Adverse Effects	• *Warnings*: QTc prolongation, ASCVD/DM • *Common*: hot flashes, increased TGs, glucose, increased AST/ALT, fatigue, musculoskeletal pain

Relugolix [package insert]. Brisbane, CA: Myovant Sciences, Inc.; 2020.

HERO: Design

- Oral relugolix for androgen-deprivation therapy in advanced prostate cancer
- Randomized, open-label, phase 3 trial

Population

- Adenocarcinoma of the prostate
- Candidates for ≥ 1 year of ADT
- PSA/clinical relapse after curative-intent local intervention OR
- De novo mCSPC OR
- Advanced local disease unlikely to be cured with local intervention

Randomization (2:1)

- Relugolix 120 mg PO daily
- Leuprolide 22.5 mg IM q3mo

Endpoints

- 1°: Sustained testosterone suppression to castrate levels, day 29-48 weeks
- 2°: non-inferiority, Day 4 castrate testosterone levels, Day 15 profound castrate levels

Shore N et al. New Engl J Med. 2020; 382:2187-96.

HERO: Results

Baseline characteristics	• N = 934 (rel n=622, leu n=308) • North American (28.9%) • Mean baseline PSA (104.2 ng/mL, 68.6 ng/mL) • Presence of 1 CV risk factor (91.6%, 94.2%)

Efficacy	• 1°: castrate testosterone levels through 48 weeks
	  • 96.7% v. 88.8% (95% CI, 4.1 to 11.8; p<0.001)
	• 2°:
	  • Probability of castration on Day 4: 56% v. 0%
	  • Probability of castration on Day 15: 98.7% v. 12%
	  • Profound suppression (<20 ng/dL) on Day 15: 78.4%% v. 1.0%

Safety	• Hot flash (54.3% v. 51.6%) • Diarrhea (12.2% v. 6.8%) • LFT elevations (1.4% v. 1.3%) • **Major adverse CV events (MACE) (2.9% v. 6.2%)**
Questions	• Cost effectiveness • Who are the best candidates for relugolix?

Shore N et al. New Engl J Med. 2020; 382:2187-96.

Tivozanib (Fotivda®)

- Approved March 10, 2021
- Adults with relapsed or refractory advanced RCC following ≥ 2 previous therapies

Mechanism of Action	Selective VEGFR tyrosine kinase inhibitor
Dosing	1.34 mg once daily on days 1-21 of a 28 day cycle
PK/DDIs	• Major substrate of CYP 3A4 • t ½ = 111 hours
Adverse Effects	• *Warnings*: hypertension, cardiac, hemorrhage, proteinuria, RPLS, VTE, thyroid dysfunction, wound healing complications • *Common*: PPE (16%), diarrhea (35%), stomatitis (20%), dysphonia (23%), LFT & SCr elevation

Fotivda [package insert]. Boston, MA: Aveo Pharmaceuticals, Inc.; 2021.

Challenges in mRCC*

- Salvage after improved front-line therapies (e.g. Immune checkpoint inhibitors (ICI) + VEGFR combinations)
- Many off-target adverse effects with VEGFR TKIs
- Lack of guidance for 3rd & 4th line therapies

*See Appendix 1 for review of mRCC therapy options

TIVO-3: Design

- Tivozanib versus sorafenib in patients with advanced RCC: a phase 3, multicentre, randomized, controlled, open-label study

Population

- mRCC
- 2+ prior therapies (≥1 VEGFR TKI other than sorafenib)
- Measurable disease on RECIST
- ECOG 0 or 1

Randomization

Tivozanib 1.5 mg PO daily

Sorafenib 400 mg PO BID

Endpoints

- 1°: PFS
- 2°: OS, objective response, duration of response, safety

Rini B et al. Lancet Oncol. 2020; 21:95-104.

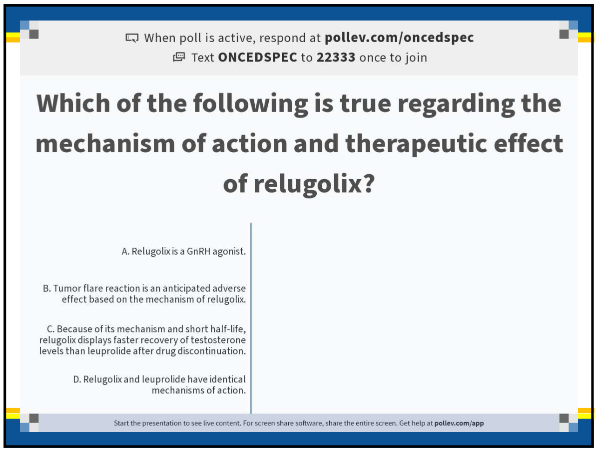
TIVO-3: Results

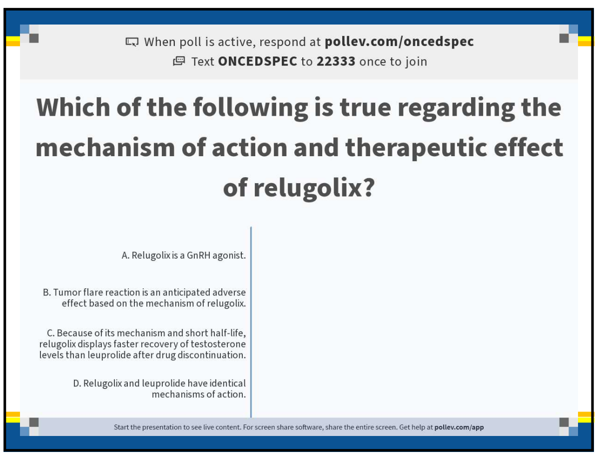
Baseline characteristics	• N = 350 (tivo n=175, soraf n=175) • Male (72%, 73%) • Clear cell (94%, 91%) • Favorable risk (19%, 21%), IM risk (62%, 60%), poor risk (18%, 34%) • 2 previous therapies (62%, 59%) • ICI+VEGFR TKI (27%, 25%), 2 VEGFR TKIs (45%, 46%)

Efficacy	• PFS
	  • 5.6 mo v. 3.9 mo (HR 0.73, 95% CI 0.56-0.94; **p=0.016**)
	• OS
	  • 16.4 mo v. 19.7 mo (HR 0.99, 95% CI 0.76-1.29; p=0.95)
	• ORR: 18% v. 8%
	• Duration of response: NR v. 5.7 mo.

Safety	• Serious AEs (G3/4): 11% v. 10% • Dose interruptions/reductions: 48%/24% v. 63%/38% • More fatigue, hypertension, nausea, dysphonia, and skin toxicity with tivo
Questions	How is this drug going to be used?

Rini B et al. Lancet Oncol. 2020; 21:95-104.


When poll is active, respond at pollev.com/oncedspec
Text ONCEDSPEC to 22333 once to join
Which of the following is true regarding the mechanism of action and therapeutic effect of relugolix?
A. Relugolix is a GnRH agonist.
B. Tumor flare reaction is an anticipated adverse effect based on the mechanism of relugolix.
C. Because of its mechanism and short half-life, relugolix displays faster recovery of testosterone levels than leuprolide after drug discontinuation.
D. Relugolix and leuprolide have identical mechanisms of action.
Start the presentation to see live content. For screen share software, share the entire screen. Get help at pollev.com/app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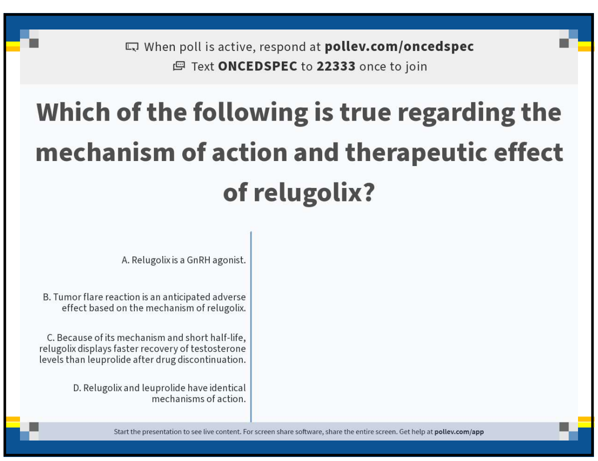
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- Genitourinary
- Breast + Gyn
- Lung
- Miscellaneous

Breast + Gynecologic

1. Margetuximab-cmkb (Margenza®) – HER2+ metastatic breast cancer
2. Dostarlimab (Jemperli®) – advanced endometrial with mismatch repair deficient (dMMR)

Margetuximab (Margenza®)

- Approved December 16, 2020
- Adults with metastatic HER2+ breast cancer, in combination with chemotherapy, who have received 2+ lines of anti-HER2 therapy (≥1 for metastatic disease)

Mechanism of Action	Anti-HER2 monoclonal antibody; Fc optimized to increase affinity and ADCC
Dosing	15 mg/kg IV every 3 weeks in combination with chemotherapy
PK/DDIs	• Catabolism to small peptides + AAs • Anthracyclines (cardiotoxicity)
Adverse Effects	• *Warnings*: cardiotoxicity (higher in elderly), infusion-related reactions • *Common*: infusion-related reactions (13.3%), minimal emetic potential, increased SCr (68%)

Margenza [package insert]. Rockville, MD. MacroGenics, Inc., 2020.

SOPHIA: Design

- Efficacy of margetuximab vs trastuzumab in patients with pretreated ERBB2-positive advanced breast cancer
- Phase 3, randomized, open-label trial

Population

- Advanced HER2+ breast cancer
- Progressive disease after 2+ lines ofanti-HER2 therapy, including pertuzumab
- 1-3 lines of nonhormonal metastatic BC therapy
- ECOG 0-1

Randomization

- Margetuximab 15 mg/kg IV q3w + chemo
- Trastuzumab 6 mg/kg (8 mg/kg load) q3w + chemo

Endpoints

- 1°:
  - PFS
  - OS
- 2°:
  - ORR

Rugo H et al. JAMA Oncol. 2021;7(4):573-584.

SOPHIA: Results

Baseline characteristics	• N = 536 (marg n=266, trastuz n=270) • Median age = 55, 56 years • > 2 metastatic sites = 51.9%, 53.3% • ER/PR+ = 59.4%, 53.7% • >2 prior therapies = 34.2%, 33.3% • Trastuzumab (100%), pertuzumab (100%, 99.6%), ado-trastuzumab emtansine (91%, 91.5%), lapatinib (15.4%, 14.4%) • Chemo choice = vinorelbine (35.6%), capecitabine (26.7%), eribulin (4%), gemcitabine (12.3%)
Efficacy	• PFS: • **5.8 mo v. 4.9 mo (HR 0.76; 95% CI, 0.59-0.98; p = 0.03)** • OS: 26.1 mo v. 19.8 mo (HR 0.89; 95% CI, 0.69-1.13; p = 0.33) • ORR: 22% v. 16% (p = 0.06)
Safety (all grade)	• Fatigue: 42% v. 35.3% • Infusion reactions: 13.3% v. 3.4% • Many AEs likely related to chemo backbone
Questions	• Will this approval change practice? • What further studies would be helpful to answer this question?

Rugo H et al. JAMA Oncol. 2021;7(4):573-584.

Dostarlimab (Jemperli®)

- Approved April 22, 2021
- Adults with mismatch repair deficient (dMMR) recurrent or advanced endometrial cancer after progression/following a prior platinum-containing regimen

Mechanism of Action	Anti-PD-1 monoclonal antibody
Dosing	500 mg IV every 3 weeks x 4 doses, followed by 1 g IV every 6 weeks
PK/DDIs	• Catabolism to small peptides + AAs • Corticosteroids
Adverse Effects	• *Warnings*: **immune-related adverse events**, infusion-related reactions • *Common*: fatigue (46%), endocrine and metabolic (↓Ca, K, Na), diarrhea (26%), pruritis (14%), increased LFTs (15-25%), minimal emetic potential

Jemperli [package insert]. Research Triangle Park, NC. GlaxoSmithKline, 2021.

GARNET: Design

- Clinical activity and safety of the anti-programmed death 1 monoclonal antibody dostarlimab for patients with recurrent or advanced dMMR endometrial cancer: a nonrandomized phase 1 clinical trial

Population

- Advanced or recurrent dMMR EC
- ≤ 2 prior lines of treatment
- No prior ICI

→ Dostarlimab 500 mg IV q3w x 4, followed by 1g IV q6w →

Endpoints

- ORR
- Duration of response

Oaknin A et al. JAMA Oncol. 2020;6(11):1766-1772.

GARNET: Results

Baseline characteristics	• N = 71 • Median age = 64 years • 49% FIGO Stage III or IV disease at diagnosis • 70.4% Type 1 EC • Previous surgery (90.1%), radiation (78.9%), chemotherapy (100%)

Efficacy	• ORR = 30 patients (42.3%)
	  • Response ongoing 25/30 (83.3), duration of response NR
	  • CR = 9 (12.7%)
	  • PR = 21 (29.6%)
	  • SD = 11 (15.5%)

Safety	• Grade ≥ 3 AE: 46.2% (10.6% leading to withdrawal) • Fatigue = 14.4% • Pruritis = 9.6% • Anemia = 6.7% • Diarrhea = 15.4% • Hypothyroidism = 8.7%
Questions	• Why not use pembrolizumab?

Oaknin A et al. JAMA Oncol. 2020;6(11):1766-1772.

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Which of the following is a notable limitation of the SOPHIA trial evaluating margetuximab for previously-treated metastatic HER2+ breast cancer?

A. Comparator group containing anti-HER2 monotherapy

B. Not all patients received trastuzumab in a previous line of therapy

C. Treatment arms were not balanced in regard to number of metastatic sites

D. Study included HR+/HER2-negative patients

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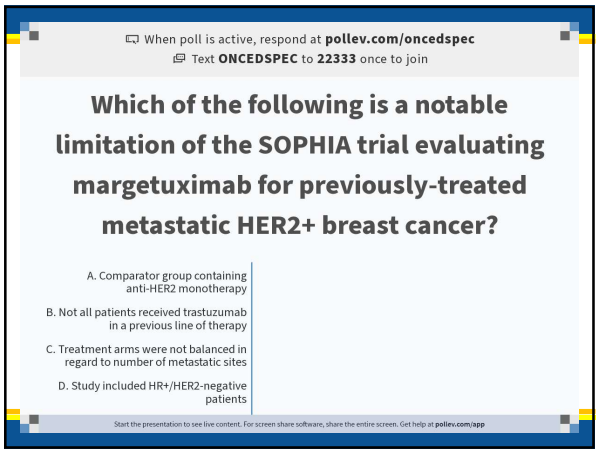
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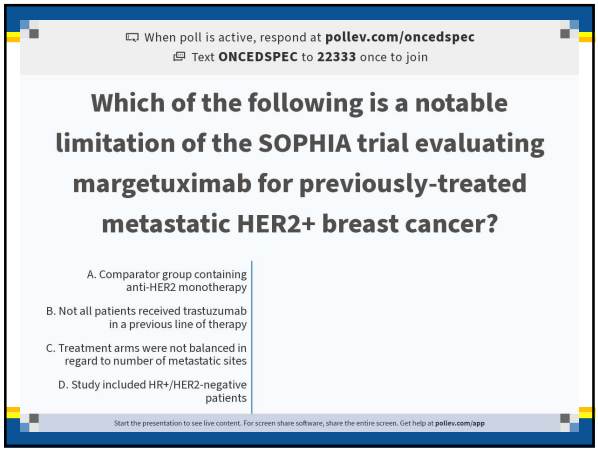
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Choose your own adventure!
Genitourinary
Breast + Gyn
Lung
Miscellaneous

Lung

1. Tepotinib (Tepmetko®) – NSCLC with MET exon 14 skipping
2. Amivantamab-vmjw (Rybrevant®) – NSCLC with EGFR exon20ins
3. Sotorasib (Lumakras®) – NSCLC with KRAS G12C mutation

Tepotinib (Tepmetko®)

- Approved February 3, 2021
- Adults with newly-diagnosed or previously-treated metastatic NSCLC with MET exon 14 skipping alterations

Mechanism of Action	Selective MET tyrosine kinase inhibitor
Dosing	450 mg PO daily with food
PK/DDIs	• pKa = 9.5 (food increases absorption) • Minor substrate of CYP 3A4 • Minor substrate, and inhibitor of Pgp
Adverse Effects	• Warnings: hepatotoxicity, pulmonary toxicity • Common: edema (4-70%), ↑K (25%), minimal or low emetic potential, LFT elevations (35-50%)

Tepmetko [package insert]. Rockland, MA. EMD Serono, Inc., 2021.

VISION: Design

- Tepotinib in non-small-cell lung cancer with MET exon 14 skipping mutations
- Phase 2, open-label study

Population
- Advanced or metastatic NSCLC
- MET exon 14 skipping mutation

→ Tepotinib 500 mg once daily →

Endpoints
- ORR
  - By liquid or tissue biopsy

Paik P et al. N Engl J Med. 2020;383:931-43.

VISION: Results

Baseline characteristics	• N = 99 • Liquid biopsy 67%, Both liquid and tissue 27% • Median age = 74 years • Metastatic disease at entry 97% • Previous treatment = 57% • ICI = 46%

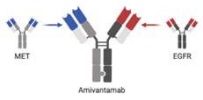
Efficacy	• ORR = 46% (all PR)
	  • Liquid biopsy ORR = 48%
	  • Tissue biopsy ORR = 50%
	• Median duration of response = 11.1 months

Safety (all grades)	• AE leading to discontinuation 7% • Edema 63% • Nausea 26% • Diarrhea 26% • SCr inc 18% • Pleural effusion 8% • AST/ALT increased 7%
Questions	• How will this be used in practice compared with capmatinib?

Paik P et al. N Engl J Med. 2020;383:931-43.

Amivantamab (Rybrevant®)

- Approved May 21, 2021
- Adults with locally advanced or metastatic NSCLC with EGFR exon 20 insertion mutations, whose disease have progression after platinum-based chemotherapy



Mechanism of Action	Bispecific anti-EGFR and MET monoclonal antibody
Dosing	<80kg: 350 mg IV on Day 1, 700 mg IV on Day 2, then 1,050 mg IV once weekly x 3 weeks, then 1,050 mg IV q2w ≥80kg: 350 mg IV on Day 1, 1,050 mg IV on Day 2, then 1,400 mg IV once weekly x 3 weeks, then 14,00 mg IV q2w *diphenhydramine, acetaminophen, and corticosteroid pre-medication required
PK/DDIs	• None significant
Adverse Effects	• Warnings: acneiform rash, infusion reactions, ocular toxicity, photosensitivity, pulmonary toxicity • Common: edema (27%), paronychia (50%), rash (84%), diarrhea (16%), stomatitis (26%), ↓Mg, Ph, K, Na, LFT elevations (MET), ↑SCr

Rybrevant [package insert]. Horsham, PA. Janssen Biotech, Inc., 2021.
Image created with Biorender

CHRYSALIS: Design

- Amivantamab in EGFR exon 20 insertion-mutated non-small cell lung cancer progressing on platinum chemotherapy: initial results from the phase I study
- Phase 1, open-label, dose-escalation and dose-expansion study

Population
- Metastatic or unresectable NSCLC progressed on or ineligible for SOC therapy
- Qualifying EGFR or MET mutation (exon20del = Cohort D)
- ECOG 0 or 1

→ Amivantamab IV standard dose based on BW →

Endpoints
- Dose-limiting toxicity
- ORR

Park K et al. J Clin Oncol. 2021;epub DOI https://doi.org/10.1200/JCO/21/00662

CHRYSALIS: Results

Baseline characteristics	• N = 81 • Median age = 62 years • 49% Asian • Median lines of therapy = 2
Efficacy	• ORR = 40% (4% CR, 36% PR, 48% SD)
Safety	• AE leading to discontinuation 7% • Rash 86% • IRR 66% • Paronychia 45% • Stomatitis 21% • Pruritis 17% • Diarrhea 14% • ILD 4%
Questions	• Will this drug be warranted in the long run with a confirmatory study? • Will less arduous dosing strategies become available?

Park K et al. J Clin Oncol. 2021;epub DOI https://doi.org/10.1200/JCO/21/00662

Sotorasib (Lumakras®)

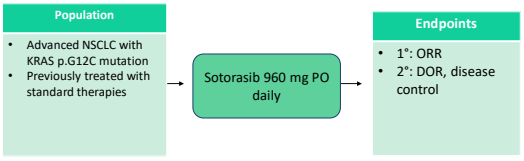
- Approved May 28, 2021
- Adults with KRAS G12C-mutated locally advanced or metastatic NSCLS who have received at least 1 prior systemic therapy

Mechanism of Action	Specific RAS tyrosine kinase inhibitor
Dosing	960 mg PO daily
PK/DDIs	• Nonenzymatic conjugation and oxidative metabolism via CYP3As • Major substrate of CYP 3A4 • Moderate inducer of CYP 3A4 • Absorption increased with high fat meal; avoid PPIs/H2RAs
Adverse Effects	• Warnings: hepatotoxicity, pulmonary toxicity • Common: edema (15%), rash (12%), ↓Ca, Na, minimal or low emetic potential, LFT elevations (25-39%), fatigue, arthralgias

Lumakras [package insert]. Thousand Oaks, CA. Amgen Inc., 2021.

CodeBreaK100: Design

- Sotorasib for lung cancers with KRAS p.G12C mutation
- Phase 2, single-arm trial



Skoulidia F et al. N Engl J Med. 2021 Jun 24;384(25)2371-2381.

CodeBreaK100: Results

Baseline characteristics	• N = 126 • Received platinum therapy and ICI = 81%
Efficacy	• ORR =37.1% (CR 3.2%, PR 33.9%) • Median duration of response = 11.1 months • Disease control = 80.6% • Median PFS = 6.8 months • Median OS = 12.5 months
Safety	• TRAE = 69.8% • Grade 3+ = 20.1% • Hepatotoxicity = 1.7% • ILD/pneumonitis = 0.6% • ≥20%: diarrhea, MSK pain, nausea, fatigue, cough
Questions	• Confirmatory Phase 3 studies?

Skoulidia F et al. N Engl J Med. 2021 Jun 24;384(25)2371-2381.

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Which newly-approved drugs for NSCLC target mesenchymal-epithelial transition (MET)?

A. Amivantamab and sotorasib
B. Sotorasib
C. Amivantamab and tepotinib
D. Tepotinib

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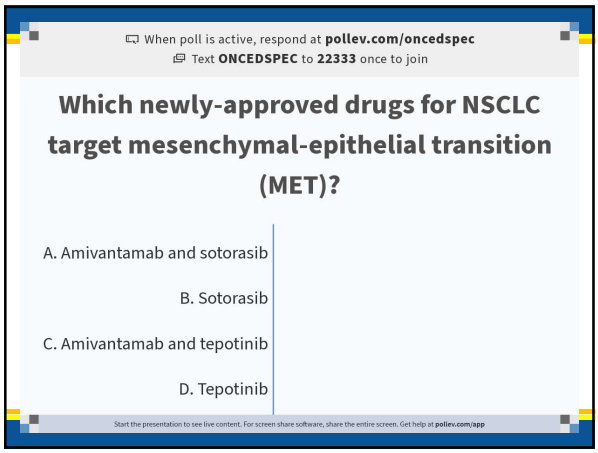


Choose your own adventure!

- Genitourinary
- Breast + Gyn
- Lung
- Miscellaneous

Miscellaneous

1. Pralsetinib (Gavreto®) – advanced or metastatic RET-altered thyroid and lung cancers
2. Infigratinib (Truseltiq®) – cholangiocarcinoma with FGFR-2 alteration

Pralsetinib (Gavreto®)

- Approved December 1, 2020
  - Adults and pediatric patients ≥ 12 years with advanced or metastatic RET-mutated medullary thyroid cancer OR RET fusion-positive thyroid cancer who are radioactive iodine-refractory
  - Adult patients with RET fusion-positive mNSCLC

Mechanism of Action	RET tyrosine kinase inhibitor (& many others, including VEGFR, FGFR2, and JAK2)
Dosing	400 mg PO daily on an empty stomach
PK/DDIs	• Major substrate of CYP 3A4 • Minor substrate of CYP1A2 and 2D6 • Minor substrate of Pgp • Cmax and Tmax increased by food
Adverse Effects	• Warnings: bone marrow suppression, hemorrhage, hepatotoxicity, hypertension, pulmonary toxicity, TLS (MTC), wound healing impairment • Common: edema (20-29%), hypertension (28-40%), rash (24%), electrolyte abnormalities, minimal to low emetic potential, myelosuppression (G3 3-16%), peripheral neuropathy (20%), ↑ SCr, CK

Gavreto [package insert]. Cambridge, MA. Blueprint Medicines Corporation. 2020.

ARROW: Design

- Phase 1/2 Study of the Highly-selective RET Inhibitor, Pralsetinib (BLU-667), in Patients With Thyroid Cancer, Non-Small Cell Lung Cancer, and Other Advanced Solid Tumors (ARROW)
- Multi-cohort, open-label, phase 1 & 2 study

Population
- Unresectable, advanced RET-altered solid tumor per local assessment (9 Groups)

→ Pralsetinib 400 mg PO daily →

Endpoints
- Phase 1: MTD
- Phase 2:
  - ORR
  - DOR

MTD: maximum tolerated dose

Gainor J et al. Lancet Oncol. 2021; 22: 959-69.

ARROW: Results

NSCLC	
Patient pop.	RET-fusion positive mNSCLC, previously treated
N	87
ORR (%)	57
DOR	NE, 80% ≥6 months
Patient pop.	RET-fusion position mNSCLC, treatment naïve
N	27
ORR (%)	70
DOR (mo.)	9, 58% ≥6 months

MTC	
Patient pop.	RET-mutated MTC, previously treated
N	55
ORR (%)	60
DOR (mo.)	NR, 79% ≥6 months
Patient pop.	RET-mutated MTC, treatment naïve
N	29
ORR (%)	66
DOR (mo.)	NR, 84% ≥6 months

RET-fusion thyroid	
Patient pop.	RET-fusion positive thyroid cancer, previously treated with radioactive iodine
N	9
ORR (%)	89 (all PR)
DOR (mo.)	NR, 100% ≥6 months

MTC: metastatic thyroid cancer

Gainor J et al. Lancet Oncol. 2021; 22: 959-69.

Infigratinib (Truseltiq®)

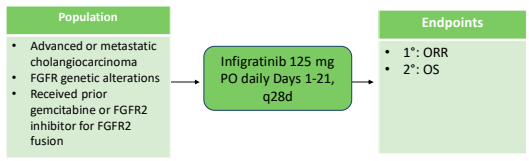
- Approved May 28, 2021
- Adults with previously treated, unresectable locally advanced or metastatic cholangiocarcinoma with FGFR2 fusion or other rearrangement

Mechanism of Action	FGFR1-3 tyrosine kinase inhibitor
Dosing	125 mg PO on an empty stomach daily for 21 days, followed by 7 days off in 28-day cycles
PK/DDIs	• Major substrate of CYP 3A4 • Absorption increased with high fat meal; avoid PPIs/H2RAs
Adverse Effects	• Warnings: ocular toxicity, hyperphosphatemia and soft-tissue mineralization, embryo-fetal toxicity • Common: ≥ 20%: nail toxicity, stomatitis, dry eye, fatigue, alopecia, PPE, arthralgia, dysgeusia, constipation, dry mouth, eyelash changes, diarrhea, dry skin

Truseltiq [package insert]. Brisbane, CA. QED Therapeutics, Inc. 2021.

CBGJ398X2204: Design

- A phase II study of infigratinib in previously treated advanced/metastatic cholangiocarcinoma with FGFR gene fusions/alterations
- Multicenter, open-label, single-arm trial



Javle M et al. J Clin Oncol. 10.1200/JCO.2021.39.3_suppl.TPS356 Journal of Clinical Oncology 39, no. 3_suppl

CBGJ398X2204: Results

Baseline characteristics	• N = 108
Efficacy	• ORR =23% (CR 1, PR 24) • 8 patients maintained response for ≥6 months • Median DOR = 5 months
Safety	• Calcium phosphate homeostasis (85.2%) • Tissue calcification (2.8%) • Pathological fracture (0.9%) • Vascular calcification/mineralization (0.9%) • Eye disorders (70.4%) • Central serous retinopathy/retinal pigment epithelial detachment–like events (16.7%)
Questions	• Place in therapy as compared with pemigatinib?

Javle M et al. J Clin Oncol. 10.1200/JCO.2021.39.3_suppl.TPS356 Journal of Clinical Oncology 39, no. 3_suppl
Cancer Network. Antitumor Effects Noted With Infigratinib in FGFR2+ Cholangiocarcinomas Refractory to Chemotherapy. Available at: https://www.cancernetwork.com/view/antitumor-effects-noted-with-infigratinib-in-fgfr2-cholangiocarcinomas-refractory-to-chemotherapy

CBGJ398X2204: Results

Useful in Certain Circumstances[f]
- For *NTRK* gene fusion-positive tumors:
  - Entrectinib[5,7]
  - Larotrectinib[8]
- For MSI-H/dMMR tumors/TMB-H tumors:
  - Pembrolizumab[6,e,9,13,14]
- For cholangiocarcinoma with *FGFR2* fusions or rearrangements:
  - Pemigatinib[15]
  - Infigratinib[16]
- For cholangiocarcinoma with *IDH1* mutations
  - Ivosidenib[17]
- For *BRAF*-V600E mutated tumors
  - Dabrafenib + trametinib [18,19]
- Nivolumab[e,20] (category 2B)
- Lenvatinib + pembrolizumab[e,21] (category 2B)

Pemigatinib	Infigratinib
• Approved 4/17/2020 • 1 tablet daily • With or without food	• Approved 5/28/21 • 2 capsules (1 x 100mg, 1 x 25mg) daily • On empty stomach • Avoid PPIs/H2RAs

NCCN. Hepatobiliary Cancers. v4.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/hepatobiliary.pdf

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Which of the following should be evaluated prior to initiating therapy with infigratinib?

A. Ensure patient discontinues concomitant acid-suppressing therapy.

B. Review NGS results to confirm FGFR fusion or rearrangement.

C. Confirm progression of disease after at least 1 prior therapy.

D. All of the above

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Appendix 1: Abbreviations

- ADT = androgen-deprivation therapy
- CR = complete response
- dMMR = mismatch repair deficient
- EC = endometrial cancer
- EGFR = epidermal growth factor receptor
- FGFR2 = fibroblast growth factor receptor 2
- GnRH = gonadotropin releasing hormone
- ICI = immune checkpoint inhibitor
- mCSPC = metastatic castration-sensitive prostate cancer
- MET = mesenchymal-epithelial transition
- NGS = next-generation sequencing
- NSCLC = non-small cell lung cancer
- ORR = overall response rate
- OS = overall survival
- PFS = progression free survival
- PPE = palmar-plantar erythrodesia
- PR = partial response
- RCC = renal cell carcinoma
- RPLS = Reversible posterior leukoencephalopathy syndrome
- SD = stable disease
- VTE = venous thromboembolism
- VEGFR = vascular endothelial growth factor
- RET = rearranged during transfection

Appendix 2

- NCCN Recommended therapy options in mRCC

<u>1L Favorable risk clear cell (Cat 1):</u>
- axitinib + pembrolizumab
- cabozantinib + nivolumab
- lenvatinib + pembrolizumab

<u>1L Poor-IM risk clear cell (Cat 1):</u>
- axitinib + pembrolizumab
- cabozantinib + nivolumab
- nivolumab/ipilimumab
- lenvatinib + pembrolimumab

<u>1L non-clear cell (Cat 1)</u>: cabozantinib, sunitinib

<u>Subsequent therapy clear cell (Cat 1):</u> cabozantinib, lenvatinib + everolimus, nivolumab, axitinib, pazopanib, sorafenib (cCt 3)

<u>Subsequent therapy non-clear cell:</u> nivolimab, pembrolizumab, lenvatinib + everolimus, bevacizumab, pazopanib

NCCN. Kidney Cancer. v1.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/kidney.pdf

Solid Tumor Drug Updates

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