

Oral Oncology Pipeline – What’s on the Horizon?

Presenter: Ryan Chandanais, MS



CE Information

- For CE credit, please visit: <https://www.lecturepanda.com/r/oncologypipeline> or scan the QR code below.
- Credit requirements must be completed within 60 days of the program activity date.
 - Upon completion, credit will be transmitted electronically to ACPE.
 - All transmitted credit will be viewable in your CPE Monitor profile within 24 hours.



Disclosures

The following financial relationships from the past 24 months have been identified and disclosed for the following faculty of this CE activity:

- Ryan Chandanais, MS
 - Employee for McKesson for which salary was received

No relevant financial relationships from the past 24 months have been identified for the following planners of this CE activity:

- Tahsin Imam, PharmD

Learning Objectives

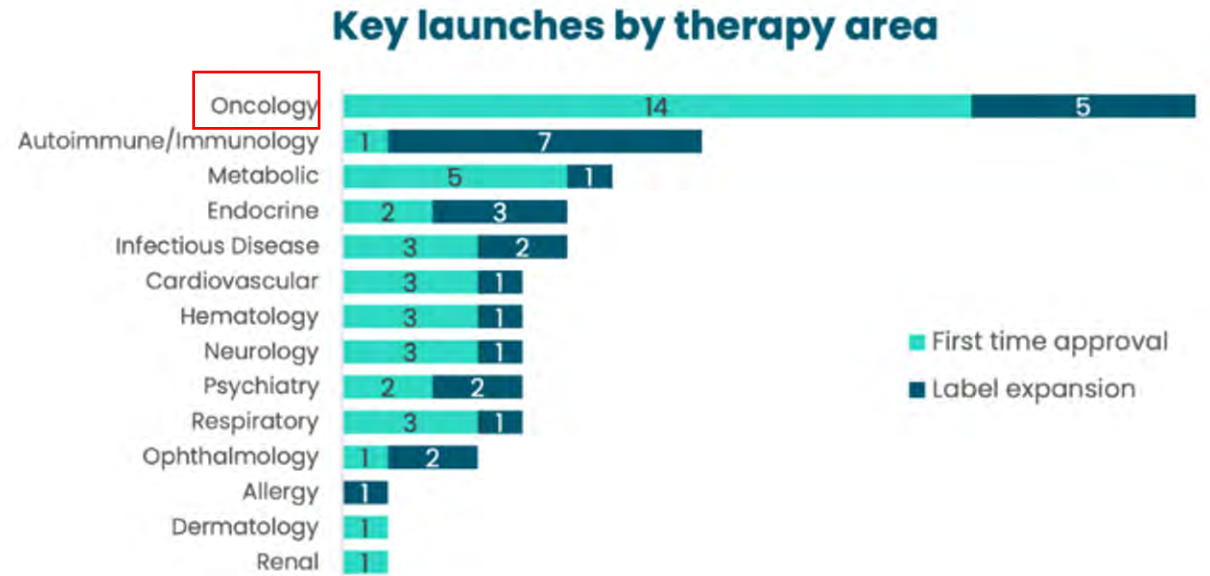
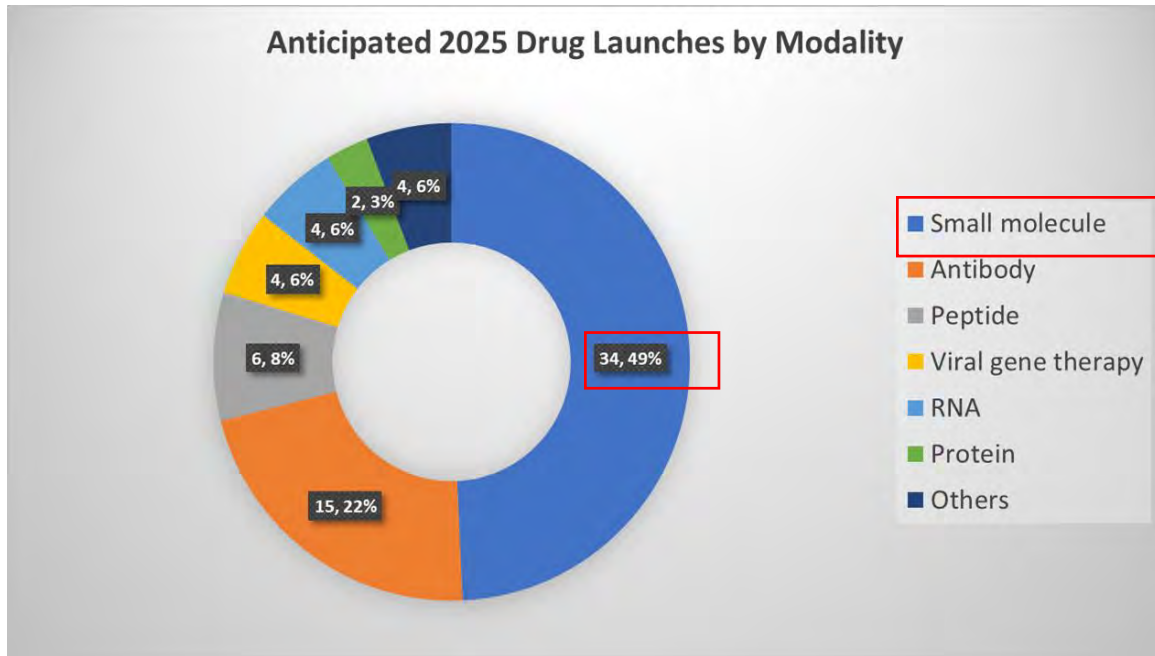
- 1. Identify emerging trends in the development of oral oncology therapies, including their increasing prevalence and impact on patient care.**
- 2. Summarize the potential clinical and operational implications of new oral therapies entering the market, with a focus on integration into Medically Integrated Dispensing (MID) workflows.**
- 3. Review potential Access / Reimbursement changes impacting oncology drugs and patient access, including those related to limited distribution networks.**
- 4. Discuss emerging data on novel oral oncology therapies, specifically those with an active New Drug Application (NDA) under FDA review or with an announced NDA submission date within the next year.**



Trends + Forecasts



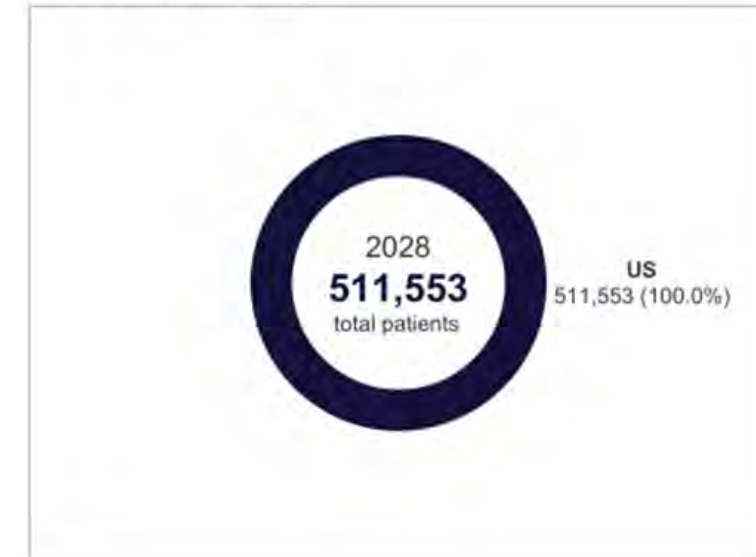
Anticipated 2025 Drug Launches: Modality + Therapy Area



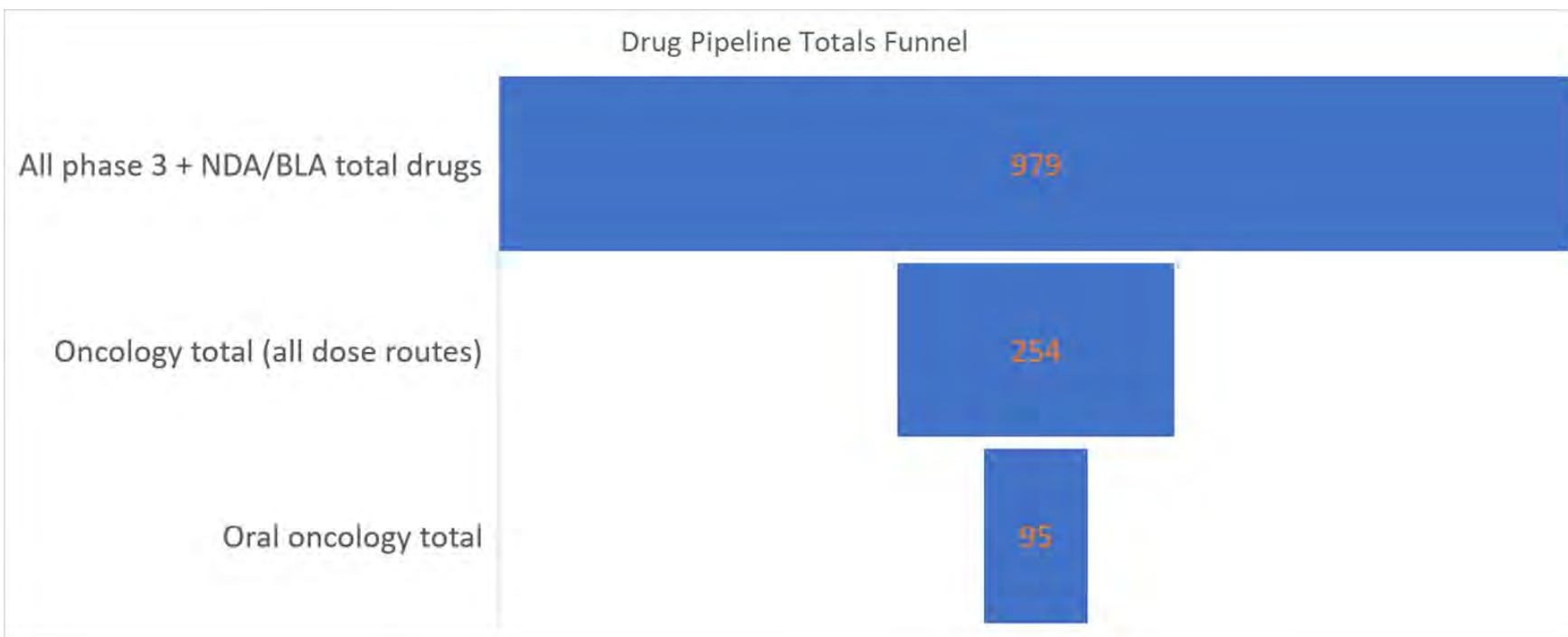
Forecasted Top 25 Oral Oncology Drugs in 2028 – Total Patients in the U.S.

Drug name	Formulation	Forecasted 2028 Patient Total - U.S.	Drug name	Formulation	Forecasted 2028 Patient Total - U.S.
Lenalidomide	Generic	47,816	Imatinib	Generic	10,978
Ribociclib	Brand	33,786	Dasatinib	Generic	9,345
Abemaciclib	Brand	24,730	Everolimus	Generic	7,959
Abiraterone	Generic	23,758	Xevinapant	Brand	7,842
Relugolix	Brand	19,802	Bendamustine	Generic	7,750
Enzalutamide	Generic	18,587	Palbociclib	Brand	7,584
Osimertinib	Brand	17,612	Lenalidomide	Brand	7,580
Venetoclax	Brand	14,507	Ibrutinib	Brand	7,353
Acalabrutinib	Brand	14,104	Palbociclib	Generic	7,332
Apalutamide	Brand	13,782	Darolutamide	Brand	6,166
Olaparib	Brand	11,898	Giredestrant	Brand	5,881
Cabozantinib	Generic	11,762	Nilotinib	Generic	5,745
Zanubrutinib	Brand	11,424			

REGIONAL ANALYSIS



Drug Pipeline Totals Funnel



Counting Methodology

- Unique drug count (drugs with trials ongoing for multiple conditions are counted only once)
- Generics are excluded

All Phase 3 + NDA/BLA total

- All disease states, dose routes, novel drugs, expanded indications (1 count), biosimilars, and 505(B)(2) agents

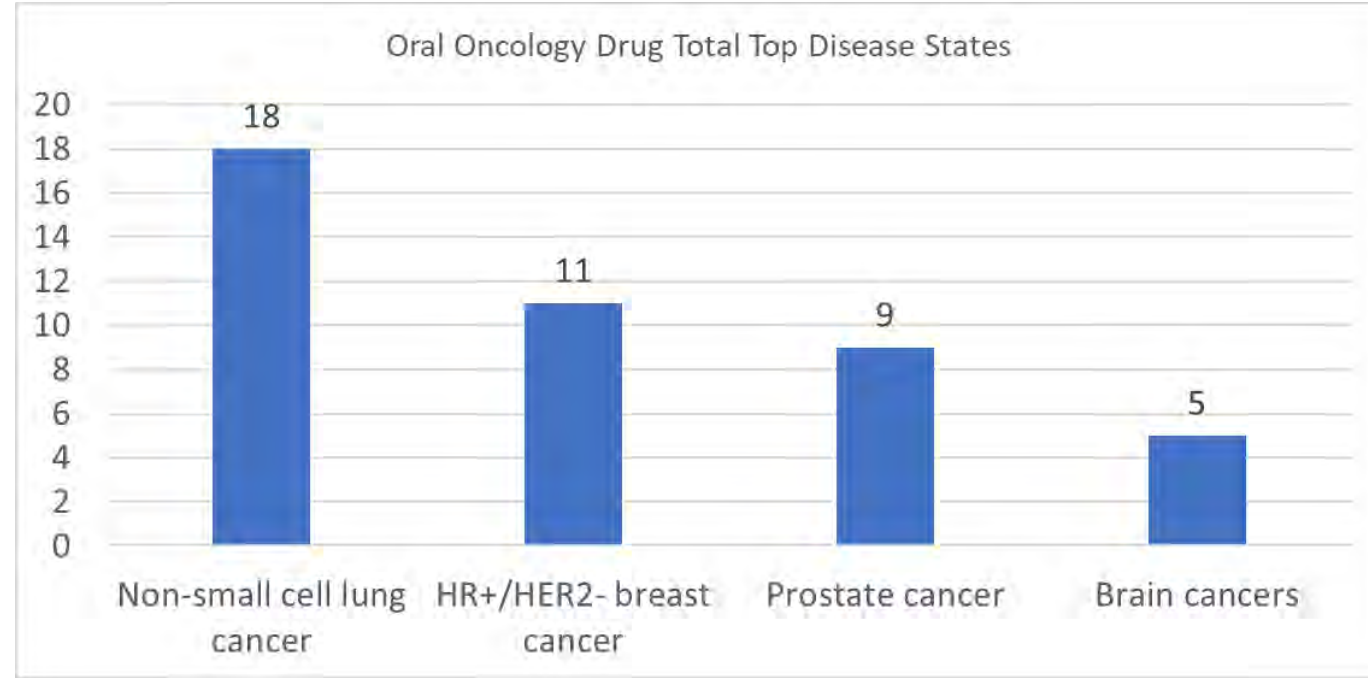
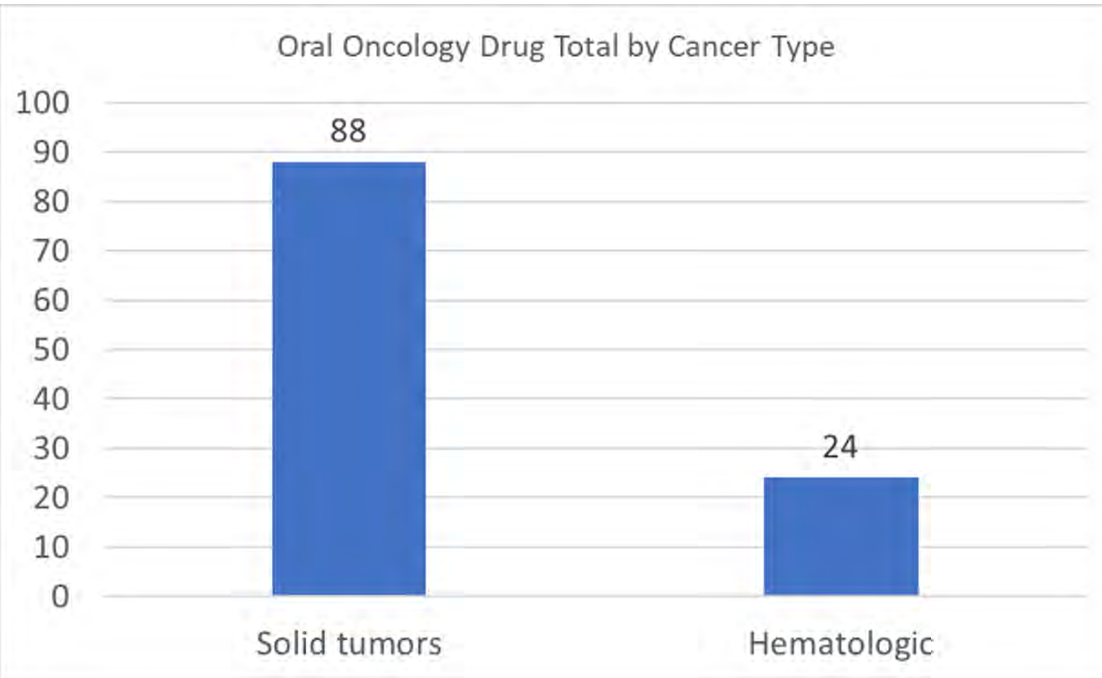
Oncology total (all dose routes)

- Same as above but includes oncology drugs only

Oral Oncology total

- Includes oncology drugs with an oral dose route only

Oral Oncology Drug Totals: Cancer Type + Top Disease States Phase 3 + NDA





Distribution + MID Pharmacy + Payer Considerations



Pharmacy Distribution Considerations

- Limited or open distribution decision is largely up to each individual manufacturer
 - Few exceptions (i.e. REMS)
- Limited distribution model for orally dosed oncology medications is predominant
- Limited distribution network size is usually proportional to patient population of disease treated

Limited distribution advantages for manufacturer

- Data availability
- Patient support programs from specialty pharmacies
 - Prior authorization navigation
 - Funding assistance coordination
 - Adherence programs
 - Scheduled calls to patients
 - Supply common adverse event support medications

Open distribution advantages for manufacturer

- Patient freedom to choose their own pharmacy (unless payer has requirements)
- Potentially lower cost (not paying for enhanced pharmacy services)

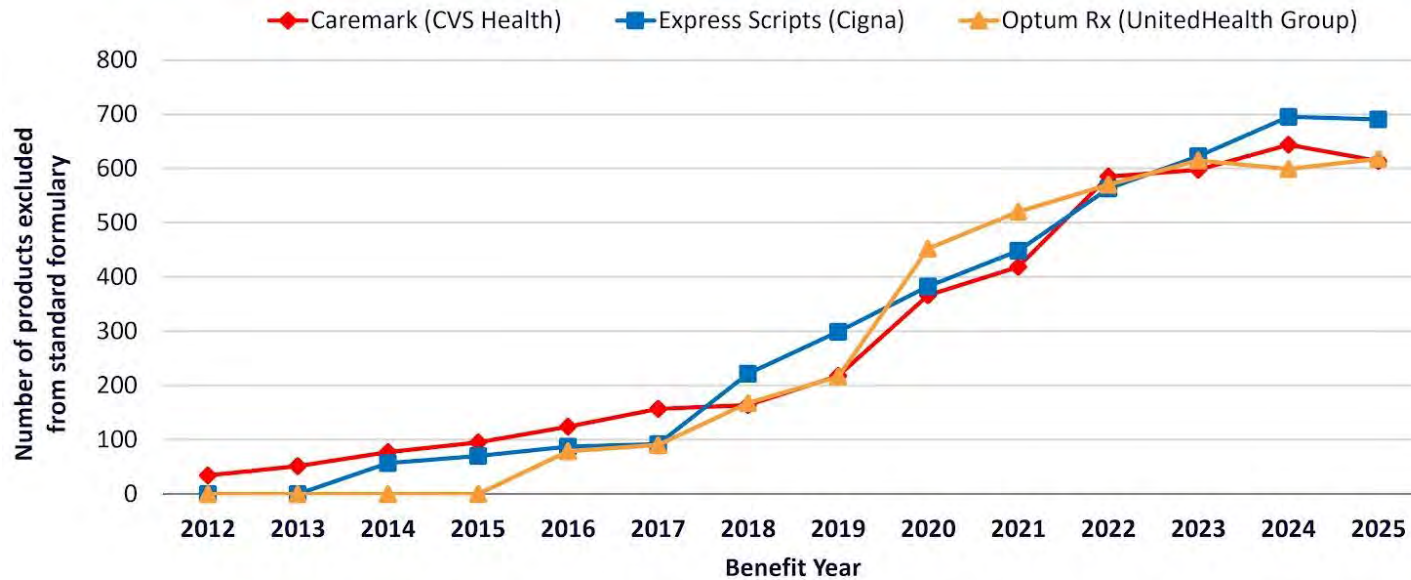
MID Pharmacy Considerations

- Open distribution oral oncology agents should be easier for MID pharmacy to manage
- Limited distribution model presents additional challenges
- Drug distribution limitation reasons
 - REMS - getting certified might allow pharmacy access
 - Manufacturer mandated - gaining access may be difficult/out of reach if not in network
- May be an opportunity for MID pharmacy to be part of a limited distribution pharmacy network
 - Better chance if limited distribution network is large
 - Manufacturers are likely to choose pharmacy partners with a national presence for small/medium network limited distribution drugs
- Additional staff and/or training may be needed
 - Replication of services provided by in-network specialty pharmacies?
- PBMs may require using their specialty pharmacy if it's in network

Lawrence L. Medically Integrated Pharmacies Can Benefit Practices, Physicians, and Patients. . ASCO Daily News.
<https://dailynews.ascopubs.org/do/medically-integrated-pharmacies-can-benefit-practices-physicians-and-patients#:~:text=Medically%20Integrated%20Pharmacies%20Can%20Benefit%20Practices%2C%20Physicians%2C%20and%20Patients,-September%2017%2C%202019&text=The%20growing%20availability%20of%20oral,The%20Practice%20and%20Patient%20Experience.%E2%80%9D>

Payer Considerations

Number of Products on PBM Formulary Exclusion Lists, by PBM, 2012 to 2025



Source: Drug Channels Institute analysis of company reports; Xcenda. Multiple formulations of a drug were counted as a single exclusion. Note that some data have been restated due to midyear additions to exclusion lists. Express Scripts did not publish exclusion lists before 2014. Optum Rx did not publish exclusion lists before 2016. Note that PBMs may exclude many of the same medications, so certain products may appear on multiple lists.

Published on *Drug Channels* (www.DrugChannels.net) on January 22, 2025.



- PBM formulary exclusions have risen substantially in the last 13 years
- Plateaued in the last 4 years
- Not specific to oral oncology
- Generally higher competition leads to greater chances for exclusions
- Oncology may be somewhat less impacted than certain other disease states due to more specific indications



Individual Pipeline Drugs

Drug selection criteria:

- Novel new orally dosed oncology agent
- NDA currently under review or with submission planned soon



Rivoceranib + Camrelizumab

- Mechanism of Action: VEGF-TKI + PD-1 inhibitor
 - Oral + IV combination therapy
- Potential Indication: Unresectable or metastatic hepatocellular carcinoma (HCC) - 1st line
- Patient Population: 467,346 patients diagnosed with HCC between 2001 to 2020
- Special FDA Designation: Orphan
- Prescription Drug User Fee Act (PDUFA) Date: 3/20/25
- Competitive Landscape: Multiple currently available treatment options
 - NCCN preferred 1st line treatment choices, metastatic setting
 - Atezolizumab + bevacizumab
 - Tremelimumab + durvalumab
 - NCCN other recommended options
 - Sorafenib
 - Lenvatinib
 - Durvalumab
 - Pembrolizumab

Biomedtracker. <https://www.biomedtracker.com/>

Abboud Y, Ismail M, Khan H, et al. Hepatocellular Carcinoma Incidence and Mortality in the USA by Sex, Age, and Race: A Nationwide Analysis of Two Decades. *J Clin Transl Hepatol.* 2024;12(2):172-181. doi:10.14218/JCTH.2023.00356

National Comprehensive Cancer Network (NCCN). Liver Cancer, 2023. <https://www.nccn.org/patients/guidelines/content/PDF/liver-hp-patient.pdf>

Rivoceranib + Camrelizumab Clinical Trial Brief

- Phase 3, CARES-310 trial, randomized, open-label, international study
- 543 patients with unresectable or metastatic HCC who had not received prior systemic therapy
- Rivoceranib (250 mg once daily) + camrelizumab (190 mg every 2 weeks) or sorafenib (400 mg twice daily)
- Analysis released at ASCO meeting, June 2024

	Rivo + Cam	Sorafenib
Median OS*	23.8 mo	15.2 mo
OS rate at 24 mo	49.0%	36.2%
OS rate at 36 mo	37.7%	24.8%
Median follow up	22.1 mo	14.9 mo
* p<0.0001		

OS: Overall survival

Taletrectinib

- Mechanism of Action: ROS1 inhibitor - 3rd generation
- Potential Indication: ROS1+ NSCLC (line agnostic)
- Patient Population: 2% of NSCLC cases are ROS1+
 - 2,000 to 4,000 newly diagnosed cases/year in the U.S.
- Special FDA Designations: Breakthrough and Orphan
- PDUFA: 6/23/25
 - Priority review
- Competitive Landscape:
 - Crizotinib
 - Entrectinib
 - Repotrectinib

Taletrectinib Clinical Trial Brief

- NDA based on pooled data from phase 2 TRUST-I and TRUST-II studies
- Multicenter, single-arm, open-label studies in patients with ROS1+ NSCLC
- Taletrectinib 400 or 600 mg once daily
- Data cutoff 3/29/24
- Median follow up of approx. 18 months

	cORR	mDOR, months	12 mo PFS	Pts w measurable brain mets
TKI naïve (n=130)	91.5%	Not reached	77.9%	17
1 prior ROS1 TKI (n=87)	54.0%	24.9	38.4%	32

cORR: confirmed objective response rate
mDOR: median duration of response
PFS: progression free survival
TEAEs: treatment emergent adverse events

- 7% discontinuation and 29% dose reduction rate attributed to TEAEs



Avutometinib + Defactinib

- Mechanisms of Action:
 - Avutometinib: RAF/MEK clamp
 - Defactinib: FAK + Pyk2 inhibitor
- Potential Indication: Recurrent low-grade serous ovarian cancer (LGSOC) with KRAS mutation in patients have received ≥ 1 prior systemic therapy
- Patient Population: 6,000 to 8,000 women in the U.S. have LGSOC
- Special FDA Designations: Breakthrough and Orphan
- PDUFA: 6/30/25
 - Priority Review and Accelerated Approval
- Competitive Landscape: Currently no FDA-approved treatments specifically for LGSOC

Avutometinib + Defactinib Clinical Trial Brief

- NDA submission based on phase II RAMP 201 study
- Adaptive, two-part, multicenter, parallel cohort, randomized, open label, with an expansion component in patients with LGSOC
- Multiple doses evaluated, moving forward with avutometinib (3.2 mg BIW) + defactinib (200 mg BID)
- At 6/30/24 data cutoff with approx. 1 year of follow up

	ORR	DOR at 6 months	PFS, months	DCR at 6+ months
All patients (n=115)	31% (23-41)	81%	12.9	61%
KRAS mutated (n=58)	44% (31-58)	87%	22.0	70%
KRAS wild type (n=57)	17% (8-30)	63%	12.8	50%

- 10% (12/115) discontinuation rate due to adverse events
- Historical SoC (chemo/hormonal treatments)
 - Response rates approx. 6-13% with PFS <12 months
 - High discontinuation rates due to adverse events

ORR: objective response rate
DOR: duration of response
PFS: progression-free survival
DCR: disease control rate

Sunvozertinib

- Mechanism of Action: EGFR inhibitor
- Potential Indication: Locally advanced non-small cell lung cancer in patients with EGFR exon 20 insertion mutations whose disease has progressed on/after platinum-based chemotherapy
- Patient Population: EGFR mutation – approx. 30% of NSCLC cases
 - Exon 20 insertion mutations – 1-10% of all EGFR mutations
- Special FDA Designation: Breakthrough
 - Priority review
- Estimated Approval Timeframe: July 2025 (NDA accepted – Jan. 2025)
 - Priority review
- Competitive Landscape: Amivantamab

Biomedtracker. <https://www.biomedtracker.com/>

Seo D, Lim JH. Targeted Therapies for EGFR 20 Exon 20 Insertion Mutation in Non-Small-Cell Lung cancer.

<https://pmc.ncbi.nlm.nih.gov/articles/PMC11172945/#:~:text=Consequently%2C%20the%20FDA%20has%20approved,progressed%20following%20platinum%2Dbased%20chemotherapy.>

Sunvozertinib Clinical Trial Brief

- WU-KONG1B - pivotal study
- Pre-treated NSCLC patients with EGFR 20 exon mutations
 - 111 patients enrolled, 107 post-platinum chemotherapy
- Sunvozertinib 300 mg once daily
- Per IRC as of 3/24/24
 - ORR 53.3%
 - mDOR not reached after 7 months follow-up
 - 66.7% were maintaining response
 - Limited description of safety profile
 - Additional press release: “The most common drug-related TEAEs were Grade 1/2 in nature and clinically manageable.”
- Investigating sunvozertinib in 1st line setting in NSCLC patients with EGFR exon20 mutation

IRC: independent review committee
ORR: objective response rate
mDOR: median duration of response
TEAE: treatment-emergent adverse event

Dordaviprone (imipridone/ONC-201)

- Mechanism of Action: Selective target for mitochondrial protease ClpP and dopamine receptor D2
- Potential Indication: Recurrent H3 K27M-mutated glioma
- Patient Population: >2,000 patients affected yearly in the U.S.
 - Most frequently occurs in children and young adults
- Special FDA Designations: Fast Track, Orphan, and Rare Pediatric Disease
- PDUFA: 8/18/25
 - Priority review
- Competitive Landscape: No FDA-approved drugs specifically for H3 K27M-mutated glioma
 - High grade glioma targeted drug treatment option: primarily temozolomide
 - With currently available treatment, median survival in H3 K27M- mutated glioma is approx. 1 year after initial diagnosis and 5.1 months from recurrence

Biomedtracker. <https://www.biomedtracker.com/>

Chimerix. Corporate Presentation 12/10/24. <https://ir.chimerix.com/static-files/9a8ee054-1b2c-4a31-8ab8-45f38074972b>

NCCN Guidelines. Brain Cancer Glioma. <https://www.nccn.org/patients/guidelines/content/PDF/brain-gliomas-patient.pdf>

Dordaviprone Clinical Trial Brief

- Phase 3 ACTION study, includes pediatric and adult patients with prior radiation therapy and potentially other prior treatments
- Dordaviprone 625 mg once weekly (adults) or adjusted dose based on body weight (pediatric patients)
- Results provided in corporate presentation on 12/10/24

n=50	RANO 2.0	RANO-HGG	RANO-LGG
ORR	28%	20%	26%
DCR	40%	40%	42%
Median time to response	4.6 mo	8.3 mo	3.6 mo
mDOR	10.4 mo	11.2 mo	10.4 mo
mOS	14.0 mo		
12-mo survival estimate	57.5%		
24-mo survival estimate	37.6%		

- 2.4% of patients experienced a treatment-related adverse event leading to modification or discontinuation of administration

ORR: objective response rate
DCR: disease control rate
mDOR: median duration of response
mOS: median overall survival

Pelabresib

- Mechanism of Action: BET inhibitor
- Potential Indication: Myelofibrosis (in combination with ruxolitinib)
- Patient Population: 13,000 patients in the U.S.
- Special FDA Designations: Fast Track and Orphan
- NDA Submission: Planned for early 2025
 - Corresponding FDA decision in late 2025/early 2026
- Competitive Landscape:
 - Pacritinib
 - Fedratinib
 - Momelotinib
 - Ruxolitinib

Biomedtracker. <https://www.biomedtracker.com/>

American Association for Cancer Research. Targeting a Rare Blood Cancer: Myelofibrosis. <https://www.aacr.org/patients-caregivers/progress-against-cancer/targeting-a-rare-blood-cancer-myelofibrosis/>

Pelabresib Clinical Trial Brief

- MANIFEST-2 study
- Pelabresib or placebo + ruxolitinib
- Pelabresib/placebo once daily in cycles of 14 days on and 7 days off
- Ruxolitinib BID in 21-day cycles
- ≥48 weeks follow up
- Results as of 3/29/24

	Pela + Rux	PBO + Rux
SVR35 at Week 48	56.5% (121/214)	37.5% (81/216)
SVR35 responders at any time	82.2% (176/214)	58.3% (126/216)
Loss of SVR35 response	13.1% (23/176)	19.8% (25/126)
≥ 1 TEAE reported (any grade)	97.6%	96.7%
≥ 1 TEAE reported (≥3 grade)	56.6%	62.1%

SVR35: ≥35% in spleen volume reduction
TEAE: treatment-emergent adverse event

Imlunestrant

- Mechanism of Action: Selective Estrogen Receptor Degradar (SERD)
- Potential Indication: HR+/HER2- breast cancer
- Patient Population: Estimated 310,720 new diagnoses of female breast cancer in 2024
 - Approx. 90% of breast cancers are HR+/HER2-
- Special FDA Designations: None
- NDA Submission: Possible in early 2025
 - Corresponding FDA decision in late 2025/early 2026
- Competitive Landscape:
 - Elacestrant
 - Fulvestrant

Biomedtracker. <https://www.biomedtracker.com/>
National Cancer Institute (NIH). Cancer Stat Facts: Female Breast Cancer Subtypes
<https://seer.cancer.gov/statfacts/html/breast-subtypes.html>
Susan G. Komen. Selective Estrogen Receptor Degradars (SERDS) for Metastatic Breast Cancer.
<https://www.komen.org/breast-cancer/metastatic/metastatic/serds-for-metastatic-breast-cancer/>

Imlunestrant Clinical Trial Brief

- Phase 3 EMBER-3 study in ER+/HER2- advanced breast cancer patients with recurrence/progression on/after an aromatase inhibitor ± CDK4/6 inhibitor with no other prior therapies
- Treatment arms: imlunestrant monotherapy (400 mg QD), imlunestrant (400 mg QD) + abemaciclib (150 mg BID), or standard of care therapy (fulvestrant or exemestane per label)

	Imlune monotherapy n=331	Imlune + abema n=213	SOC n=330
Median PFS - ESR-1 mutated	5.5 mo ¹	N/A	3.8 mo ¹
Median PFS - regardless of ESR-1 mutation status	5.5 mo ²	9.4 mo ²	N/A
ORR - ESR-1 mutated	14%	N/A	8%
Median PFS – all patients	5.6 mo ³	N/A	5.5 mo ³
ORR – all patients	12%	27%	N/A
≥3 adverse events	17.1%	48.6%	20.7%

1 and 2 – P<0.001

3 - P=0.12



Quiz



Question 1: Which drug modality has the highest number of forecasted approvals in 2025?

- **A. Small molecule**
- B. Viral gene therapy
- C. Antiviral
- D. Cell Therapy

Question 2: Which disease state has the most late-stage pipeline agents in development?

- A. Melanoma
- B. Hepatocellular carcinoma
- C. Pancreatic cancer
- **D. Non-small cell lung cancer**

Question 3: Which combination therapy is being evaluated for the treatment of recurrent low-grade serous ovarian cancer (LGSOC) ?

- **A. Rivoceranib + Camrelizumab**
- **B. Avutometinib + Defactinib**
- **C. Sunvozertib + Dordaviprone**
- **D. Xevinapant + giredestrant**

Question 4: Dordaviprone is under FDA review for the treatment of which disease state?

- A. HR+/HER2- breast cancer
- B. KRAS-mutated cancers regardless of site
- C. H3 K27M-mutated glioma
- D. Metastatic castration-resistant prostate cancer

- **Thanks for attending!**
 - **Q&A**
- **ryan.chandanais@mckesson.com**

CE Code

Oral Oncology Pipeline – What's on the Horizon?

Ryan Chandanais, MS