2020 NCODA Fall Summit

2020 Oral Oncolytic Drug Update

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#NCODASummit20

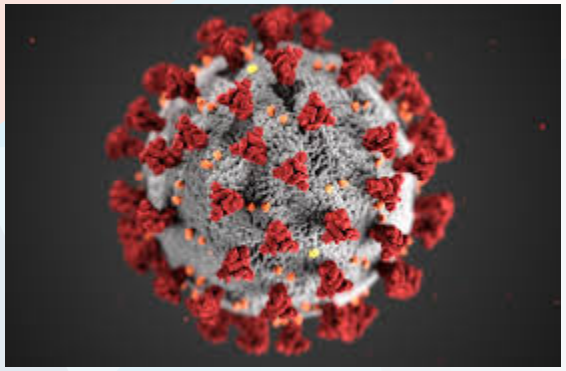
Disclosures

None to report

Learning Objective

At the end of this presentation the attendees will have a better understanding of the oral oncology agents approved by the FDA in 2020

2020…What a Year!



None of this stopped Pharma!

- 106 Original NDA & BLA Approvals
- 10 New Oral Oncolytic approvals

Ayvakit (avapritinib)

- Approved on 1/9/2020
- AYVAKIT is a kinase inhibitor indicated for the treatment of adults with unresectable or metastatic gastrointestinal stromal tumor (GIST) harboring a platelet-derived growth factor receptor alpha (PDGFRA) exon 18 mutation, including PDGFRA D842V mutations.
- Ayvakit is supplied as a tablet for oral administration. The recommended dosage of Ayvakit is 300 mg orally once daily on an empty stomach, at least 1 hour before and 2 hours after a meal. Continue treatment until disease progression or unacceptable toxicity
- Available in 100, 200 and 300mg tablets

Clinical Trials

- The FDA approval of Aykavit was based on efficacy results from the Phase 1 NAVIGATOR clinical trial, as well as combined safety results from multiple clinical trials for avapritinib.
- Patients received Ayvakit 300 mg or 400 mg orally once daily until disease progression or unacceptable toxicity.
- The trial initially enrolled patients at a starting dose of 400 mg, which was later reduced to the recommended dose of 300 mg due to toxicity.
- As there was no apparent difference in overall response rate (ORR) between patients who received 300 mg daily compared to those who received 400 mg daily, these patients were pooled for the efficacy evaluation.
- The major efficacy outcome measure was ORR based on disease assessment by independent radiological review using modified RECIST v1.1 criteria, in which lymph nodes and bone lesions were not target lesions and progressively growing new tumor nodules within a pre-existing tumor mass was progression.
- An additional efficacy outcome measure was duration of response (DOR).
- In patients with PDGFRA exon 18 mutant GIST, AYVAKIT had an overall response rate (ORR) of 84 percent, and a median duration of response (DOR) was not reached.

Clinical Trials (cont'd)

- In evaluable patients with PDGFRA Exon 18 mutant GIST:
  - The ORR was 86 percent, with three confirmed complete responses (CR) and 34 partial responses (PR; one pending confirmation).
  - The ORR was 100 percent (two CRs and three PRs; all responses were confirmed) in the first-line treatment setting.
  - The median DOR was not reached.
  - 28 patients (78 percent) remained in response as of the data cutoff date.
  - Median follow-up was 10.9 months.
- In evaluable patients with fourth-line GIST:
  - The ORR was 22 percent, with one confirmed CR and 23 PRs (one pending confirmation).
  - The median DOR was 10.2 months.
  - Median follow-up was 10.8 months.

Adverse Events

- Adverse effects associated with the use of Ayvakit may include, but are not limited to, the following:
  - edema
  - nausea
  - fatigue/asthenia
  - cognitive impairment
  - vomiting
  - decreased appetite
  - diarrhea
  - hair color changes
  - increased lacrimation
  - abdominal pain
  - constipation
  - rash
  - dizziness

Tazverik (tazemetostat)

- FDA approved 1/23/20
- TAZVERIK is a methyltransferase inhibitor indicated for the treatment of:
  - Adults and pediatric patients aged 16 years and older with metastatic or locally advanced epithelioid sarcoma not eligible for complete resection.
  - FDA approved 6/19/20:
  - Adult patients with relapsed or refractory follicular lymphoma whose tumors are positive for an EZH2 mutation as detected by an FDA-approved test and who have received at least 2 prior systemic therapies.
  - Adult patients with relapsed or refractory follicular lymphoma who have no satisfactory alternative treatment options.
- Tazverik is supplied as a 200mg tablet for oral administration. The recommended dose is 800 mg orally twice daily with or without food until disease progression or unacceptable toxicity.

Clinical Trials

- The FDA approval of Tazverik for epithelioid sarcoma was based on the results of a clinical trial enrolling 62 patients with metastatic or locally advanced epithelioid sarcoma.
- During the clinical trial, patients received 800 milligrams (mg) of Tazverik twice a day until the disease progressed or the patient reached an unacceptable level of toxicity.
- Tumor response assessments were performed every eight weeks during the clinical trial. The trial measured how many patients experienced complete or partial shrinkage (by a certain amount) of their tumors during treatment (overall response rate).
- The overall response rate was 15%, with 1.6% of patients having a complete response and 13% having a partial response. Of the nine patients that had a response, six (67%) patients had a response lasting six months or longer.
- The FDA approval of Tazverik for follicular lymphoma was based on an open-label, single-arm, multi-center Phase 2 clinical trial in patients with histologically confirmed FL whose disease had progressed following at least two prior systemic treatment regimens.
- Patients were enrolled into two cohorts: one cohort enrolled 45 patients with EZH2 activating mutations and a second cohort enrolled 54 patients with wild-type EZH2.
- All patients were treated with 800 mg of tazemetostat, administered orally twice a day.
- The major efficacy outcome measures were overall response rate (ORR) and duration of response (DOR).
- Among the 45 FL patients with an EZH2 activating mutation who received Tazverik and treated with at least 2 prior systemic therapies, the ORR was 69%, with 12% of patients achieving a complete response and 57% achieving a partial response.
- The median DOR was 10.9 months and ongoing.
- Among the 54 FL patients with wild-type EZH2 who received Tazverik and treated with at least 2 prior systemic therapies, the ORR was 34%, with 4% of patients achieving a complete response and 30% achieving a partial response. The median DOR was 13.0 months

Adverse Events

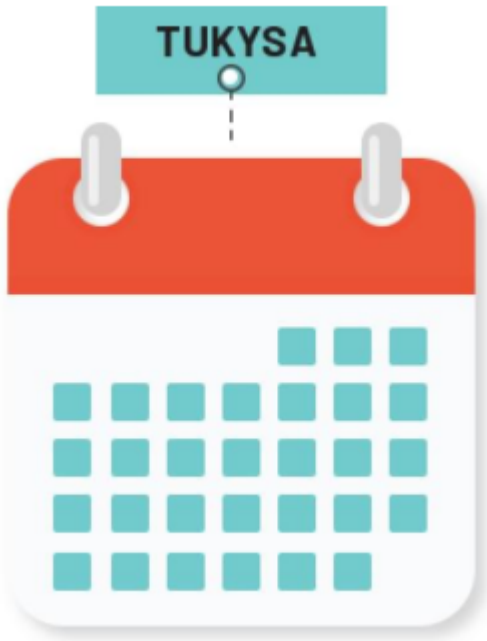
Adverse effects associated with the use of Tazverik may include, but are not limited to, the following:

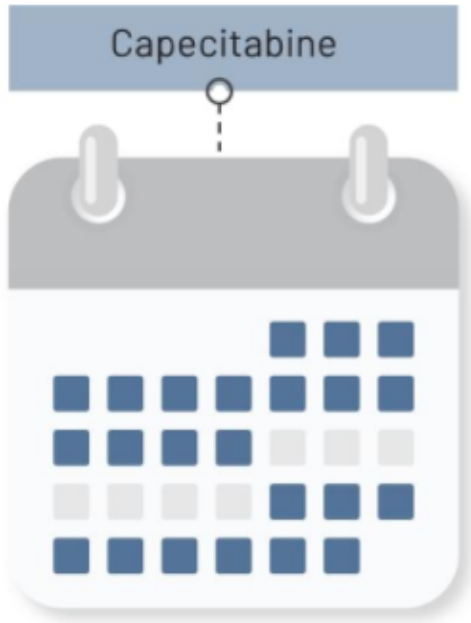
- pain
- fatigue
- nausea
- decreased appetite
- vomiting
- constipation

Tukysa (Tukatinib)

- FDA Approved 4/17/20
- TUKYSA is a kinase inhibitor indicated in combination with trastuzumab and capecitabine for treatment of adult patients with advanced unresectable or metastatic HER2-positive breast cancer, including patients with brain metastases, who have received one or more prior anti-HER2-based regimens in the metastatic setting.
- Tukysa is supplied as a 50 and a 150mg tablet for oral administration. The recommended dosage of Tukysa is 300 mg taken orally twice daily in combination with trastuzumab and capecitabine until disease progression or unacceptable toxicity.
- Advise patients to take Tukysa approximately 12 hours apart and at the same time each day with or without a meal.

Dosing



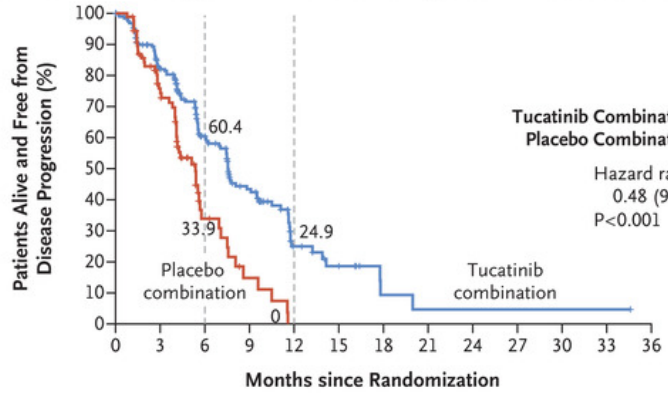


Clinical Trials

- The FDA approval of Tukysa was based on the results of HER2CLIMB, a randomized (2:1), double-blind, placebo-controlled trial enrolling 612 patients who had HER2-positive advanced unresectable or metastatic breast cancer and had prior treatment with trastuzumab, pertuzumab and ado-trastuzumab emtansine (T-DM1).
- Patients with previously treated and stable brain metastases, as well as those with previously treated and growing or untreated brain metastases, were eligible for the clinical trial, and 48% of enrolled patients had brain metastases at the start of the trial.
- The primary endpoint was progression-free survival (PFS).
- The median PFS in patients who received Tukysa, trastuzumab, and capecitabine was 7.8 months compared to 5.6 months in those patients who received placebo, trastuzumab, and capecitabine.
- Overall survival and PFS in patients with brain metastases at baseline were key secondary endpoints.
- The median overall survival in patients who received Tukysa, trastuzumab, and capecitabine was 21.9 months compared to 17.4 months in patients who received placebo, trastuzumab, and capecitabine.
- The median PFS in patients with brain metastases at baseline who received Tukysa, trastuzumab and capecitabine was 7.6 months compared to 5.4 months in patients who received placebo, trastuzumab and capecitabine.

Clinical Trials (cont'd)

A Kaplan–Meier Estimates of Progression-free Survival among Patients with Brain Metastases



	No. of Events/ No. of Patients	Median Duration (95% CI)
		mo
Tucatinib Combination	106/198	7.6 (6.2–9.5)
Placebo Combination	51/93	5.4 (4.1–5.7)

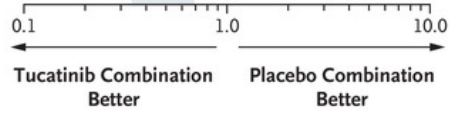
Hazard ratio for disease progression or death, 0.48 (95% CI, 0.34–0.69)
P<0.001

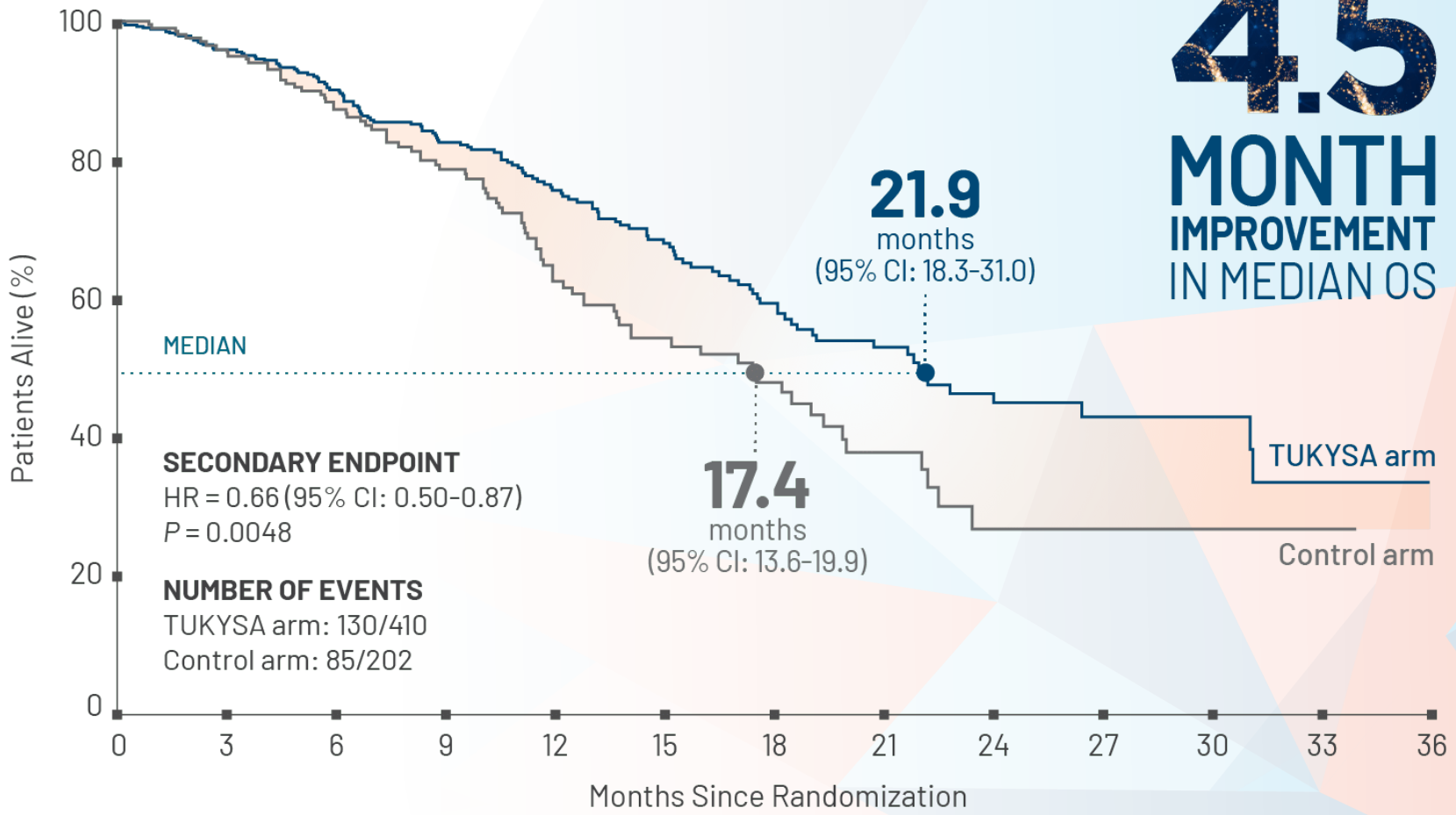
No. at Risk

Tucatinib combination	198	144	78	45	14	8	2	1	1	1	1	1	0
Placebo combination	93	49	12	4	0	0	0	0	0	0	0	0	0

B Subgroup Analysis of Progression-free Survival among Patients with Brain Metastases

Subgroup	No. of Events/ Total No.	Hazard Ratio for Disease Progression or Death (95% CI)
Total	157/291	0.48 (0.34–0.69)
Age		
≥65 yr	24/48	0.41 (0.17–1.01)
<65 yr	133/243	0.51 (0.35–0.76)
Race		
White	112/199	0.49 (0.32–0.75)
Nonwhite	45/92	0.45 (0.23–0.90)
Hormone-receptor status		
Positive for ER, PR, or both	92/166	0.48 (0.31–0.75)
Negative for ER and PR	65/125	0.50 (0.27–0.95)
ECOG performance-status score		
0	76/130	0.68 (0.41–1.15)
1	81/161	0.34 (0.21–0.55)
Geographic region		
United States and Canada	97/177	0.43 (0.27–0.67)
Rest of the world	60/114	0.60 (0.33–1.08)





NUMBER AT RISK

TUKYSA arm	410	388	322	245	178	123	80	51	34	20	10	4	0
Control arm	202	191	160	119	77	48	32	19	7	5	2	1	0

www.tukysahcp.com

Adverse Events

Adverse effects associated with the use of Tukysa may include, but are not limited to, the following:

- diarrhea
- palmar-plantar erythrodysesthesia
- nausea
- fatigue
- hepatotoxicity
- vomiting
- stomatitis
- decreased appetite
- abdominal pain
- headache
- anemia
- rash

Pemazyre (Pemigatinib)

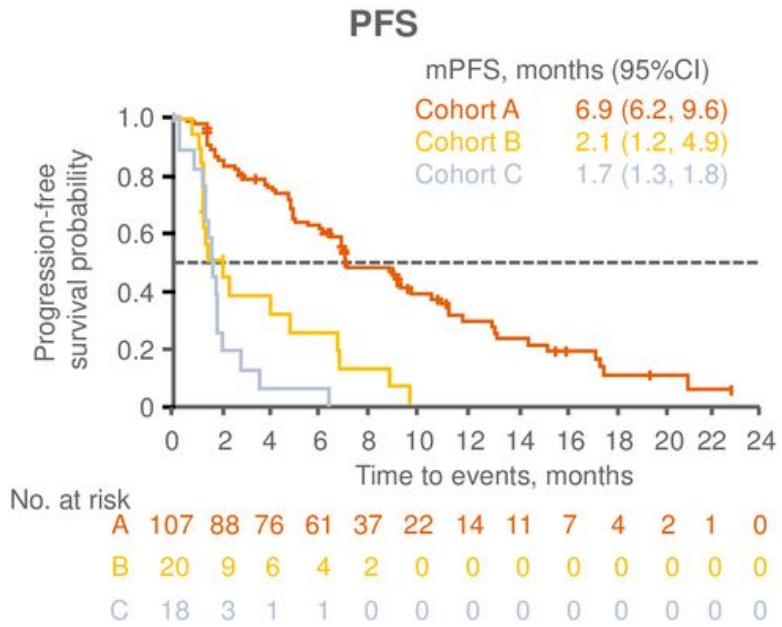
- PEMAZYRE is a kinase inhibitor indicated for the treatment of adults with previously treated, unresectable locally advanced or metastatic cholangiocarcinoma with a fibroblast growth factor receptor 2 (FGFR2) fusion or other rearrangement as detected by an FDA-approved test.
- FDA Approved 4/17/20
- Pemazyre is supplied as a 4.5, 9 & 13.5mg tablet for oral administration. The recommended dosage of Pemazyre is 13.5 mg orally once daily for 14 consecutive days followed by 7 days off therapy, in 21-day cycles. Continue treatment until disease progression or unacceptable toxicity occurs. Take Pemazyre with or without food at approximately the same time every day.

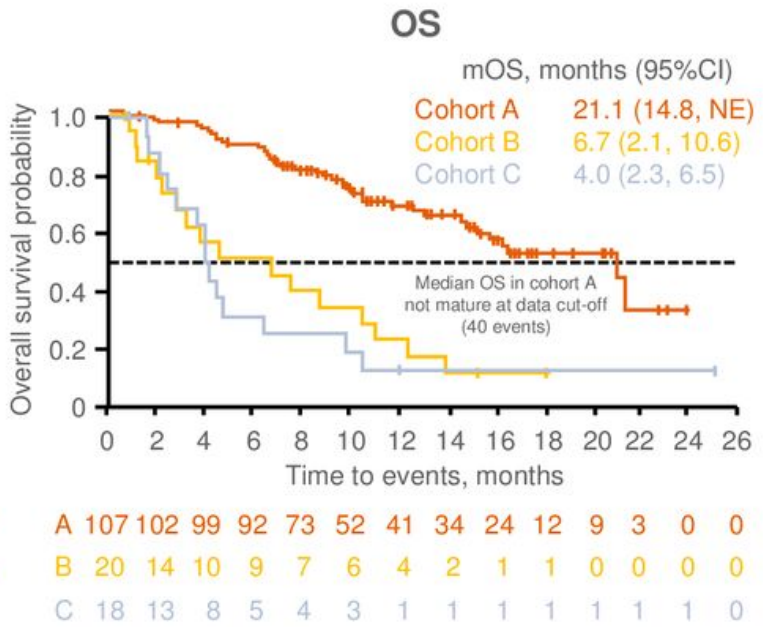
Clinical Trials

- The FDA approval of Pemazyre was based on data from FIGHT-202, a multi-center, open-label, single-arm study in adult (age ≥18 years) patients with previously treated, locally advanced or metastatic cholangiocarcinoma with documented FGFR2 fusion or rearrangement.
- Patients were enrolled into one of three cohorts – Cohort A (FGFR2 fusions or rearrangements), Cohort B (other FGF/FGFR genetic alterations) or Cohort C (no FGF/FGFR genetic alterations).
- All patients received 13.5 mg Pemazyre orally once daily (QD) on a 21-day cycle (two weeks on/one week off) until radiological disease progression or unacceptable toxicity.
- The primary endpoint of FIGHT-202 was overall response rate (ORR) in Cohort A, assessed by independent review per RECIST v1.1.
- Secondary endpoints included duration of response (DOR).
- In patients harboring FGFR2 fusions or rearrangements (Cohort A), Pemazyre monotherapy resulted in an overall response rate of 36% and median DOR of 9.1 months.

LBA40: FIGHT-202: A phase II study of pemigatinib in patients (pts) with previously treated locally advanced or metastatic cholangiocarcinoma (CCA) – Vogel A, et al

Key results (cont.)





	Cohort A	Cohort B	Cohort C
Median duration of follow-up, months (range)	15.4 (7.0–24.7)	19.9 (16.2–23.5)	24.2 (22.0–26.1)
Median duration of treatment, months (range)	7.2 (0.2–24.0)	1.4 (0.2–12.9)	1.3 (0.2–4.7)

Vogel A, et al. Ann Oncol 2019;30(suppl):abstr LBA40

Pemigatinib is a Potent and Selective Oral FGFR Inhibitor

Development program across multiple indications

pemigatinib (FGFR1/2/3)

Cholangiocarcinoma

NDA expected 2019

- 2nd-line recruitment completed
- 1st-line program recruiting (vs. gem/cis)

Bladder cancer

sNDA expected 2020

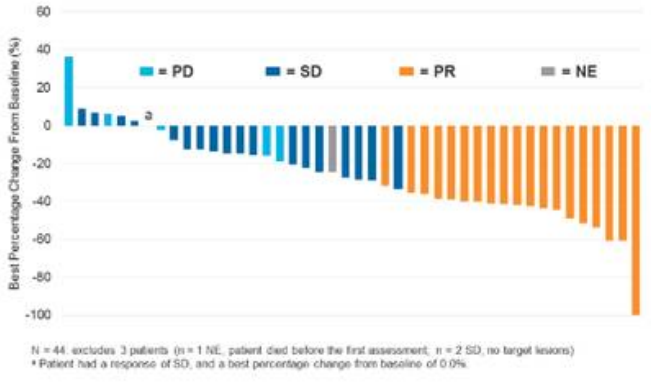
- 1st-line program in preparation (vs. chemo / PD-1)
- 2nd-line (continuous dosing) recruiting

8p11 MPN

- Ultra-rare indication
- No approved therapies for aggressive disease

2nd line cholangiocarcinoma

Intermittent dosing: ORR 40%, DCR 85%



fight-202

Hollebecque et al, ESMO 2018

Solid tumors

- Tumor-agnostic development plan
- Leverage increased availability of genetic testing

Incyte

Incyte.com

Adverse Events

Adverse effects associated with the use of Pemazyre may include, but are not limited to, the following:

- Hyperphosphatemia (60-94%)
- Alopecia (49%)
- Diarrhea (44.3%)
- Fatigue (37.2%)
- Dysgeusia (40%)
- Nausea (37.9%)
- Constipation (34.3%)
- Stomatitis (30%)
- Dry eye (26.4-34.3%)
- Dry mouth (34%)
- Vomiting (25.6%)
- Hypophosphatemia (11-30%)
- Hypercalcemia (38.9%)

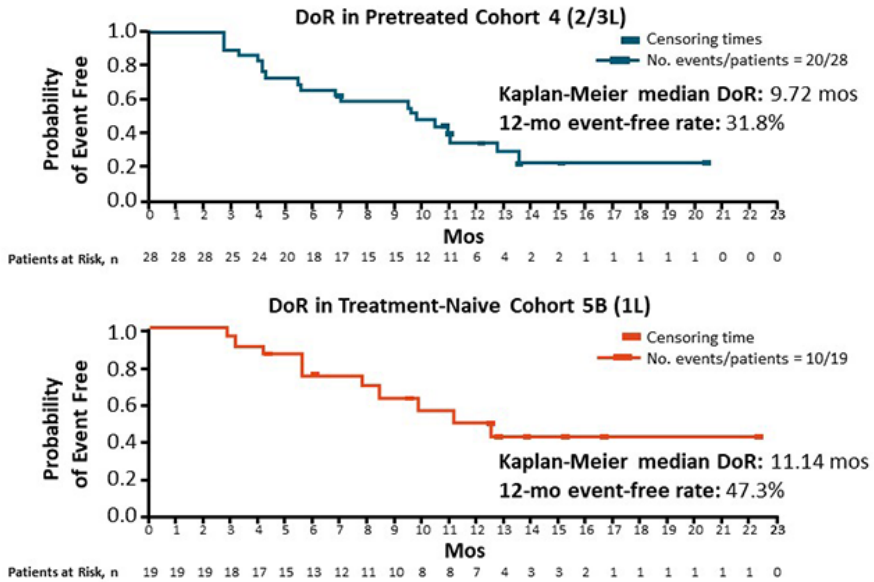
Tabrecta (Capmatinib HCl)

- FDA Approved 5/6/20
- TABRECTA is a kinase inhibitor indicated for the treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have a mutation that leads to mesenchymal-epithelial transition (MET) exon 14 skipping as detected by an FDA-approved test.
- Tabrecta is supplied as a 150 and 200mg tablet for oral administration. The recommended dosage is 400 mg orally twice daily with or without food.

Clinical Trials

- The FDA approval of Tabrecta was based on results from the pivotal GEOMETRY mono-1 Phase II multi-center, non-randomized, open-label, multi-cohort study in adult patients with EGFR wild-type, metastatic NSCLC as measured by ORR.
- The trial evaluated 97 adult patients with metastatic NSCLC harboring mutations that lead to METex14 (centrally confirmed) who were assigned to Cohorts 4 (n=69, previously treated patients) or 5b (n=28, treatment-naive), and received capmatinib tablets 400 mg orally twice daily.
- In the METex14 population (n=97), the confirmed overall response rate was 68% and 41% among treatment-naive (n=28) and previously treated patients (n=69), respectively, based on the Blinded Independent Review Committee (BIRC) assessment per RECIST v1.1.
- In patients taking Tabrecta, the study also demonstrated a median duration of response of 12.6 months in treatment-naive patients (19 responders) and 9.7 months in previously treated patients (28 responders).

GEOMETRY mono-1: Duration of Response per BIRC

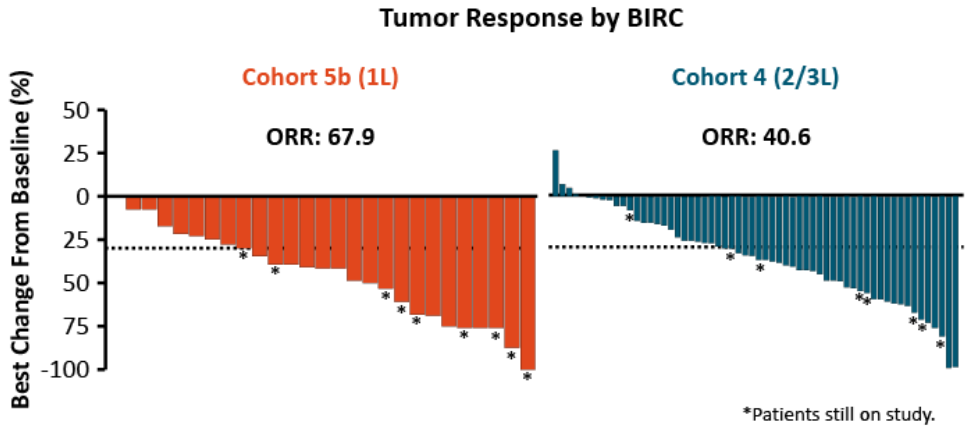


- Median DoR per BIRC:
  - Cohort 4: 9.72 mos
  - Cohort 5B: 11.14 mos
- Median DoR per investigator:
  - Cohort 4: 8.31 mos
  - Cohort 5B: 13.96 mos

Wolf. ASCO 2019. Abstr 9004.

Slid

Phase II GEOMETRY mono-1: Efficacy With Capmatinib in *MET*ex14 Mutation–Positive NSCLC



- Durability of response by BICR
  - DoR
    - 1L: 11.1 mos
    - 2L/3L: 9.7 mos
  - PFS
    - 1L: 9.7 mos
    - 2L/3L: 5.4 mos
- 54% (7/13) with intracranial response

Wolf. ASCO 2019. Abstr 9004.

Slide credit: clinicaloptions.com

Retevmo (SELPERCATINIB)

- FDA Approved 5/8/20
- RETEVMO is a kinase inhibitor indicated for the treatment of:
  - Adult patients with metastatic RET fusion-positive non-small cell lung cancer (NSCLC)
  - Adult and pediatric patients 12 years of age and older with advanced or metastatic RET-mutant medullary thyroid cancer (MTC) who require systemic therapy
  - Adult and pediatric patients 12 years of age and older with advanced or metastatic RET fusion-positive thyroid cancer who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate)
  - Retevmo is supplied as a 40 & 80mg capsule for oral administration. The recommended dosage of Retevmo based on body weight is:
    - Less than 50 kg: 120 mg
    - 50 kg or greater: 160 mg
- Take Retevmo orally twice daily (approximately every 12 hours) until disease progression or unacceptable toxicity. Retevmo may be taken with or without food unless coadministered with a proton pump inhibitor. If the patient is also taking a proton pump inhibitor, selpercatinib must be taken with food.

Clinical Trials

Retevmo was approved under accelerated approval based on overall response rate and duration of response. Continued approval for each indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s).

Accelerated Approval was based on the LIBRETTO-001 Phase 1/2 trial's endpoints of objective response rate (ORR) and duration of response (DoR). The single-arm, multi-center Phase 1/2 trial enrolled 702 patients with RET-driven cancers. The trial enrolled both treatment-naive patients and heavily pretreated patients with a variety of advanced solid tumors including RET fusion-positive NSCLC, RET-mutant MTC, RET fusion-positive thyroid cancer, and certain other solid tumors with RET alterations. Results are as follows:

RET Fusion-Positive NSCLC:

•Systemic Treatment Naïve Patients: ORR 85% and median DoR not reached at time of analysis.

•Treatment Experienced Patients: ORR 64% and median DoR 17.5 months.

RET-Mutant MTC:

•Cabozantinib/Vandetanib Naïve Patients: ORR 73% and median DoR 22 months

•Cabozantinib/Vandetanib Experienced Patients: ORR 69% and median DoR not reached at time of analysis.

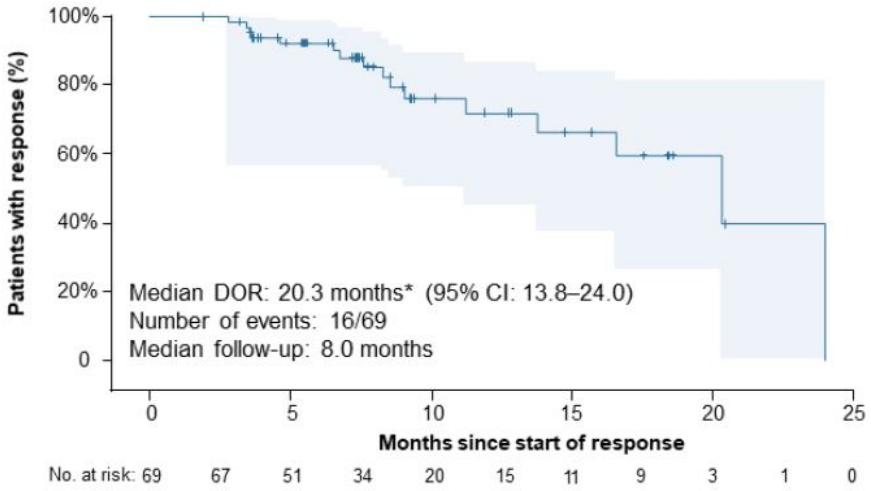
RET Fusion-Positive Thyroid Cancers:

•Systemic Treatment Naïve patients: ORR 100% and median DoR not reached at time of analysis.

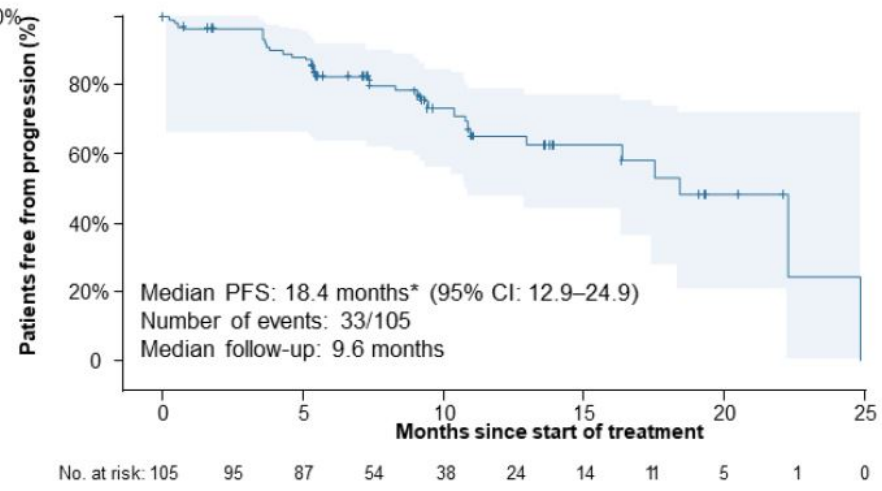
•Treatment Experienced Patients: ORR 79% and median DoR 18.4 months.

Durability of Selpercatinib Efficacy: Primary Analysis Set

Duration of response



Progression-free survival



- Of 28 patients in the PAS that progressed, 23 continued treatment post-progression, for 0.2–16.4+ months
- ORR, DOR, PFS similar regardless of prior therapy (e.g. anti-PD-1/PD-L1, MKIs)

Data cut-off: June 17th, 2019. Shading in PAS Kaplan-Meier curves indicates the 95% confidence band. *Medians are not statistically stable due to a low number of events.

Adverse Events

Adverse effects associated with the use of Retevmo may include, but are not limited to, the following:

- laboratory abnormalities
- dry mouth
- diarrhea
- increased creatinine
- increased alkaline phosphatase
- hypertension
- fatigue
- edema
- decreased platelets
- increased total cholesterol
- rash
- decreased sodium
- constipation

Qinlock (RIPRETINIB)

- FDA Approved 5/15/20
- QINLOCK is a kinase inhibitor indicated for the treatment of adult patients with advanced gastrointestinal stromal tumor (GIST) who have received prior treatment with 3 or more kinase inhibitors, including imatinib. Qinlock is supplied as a 50mg tablet for oral administration. The recommended dosage of Qinlock is 150 mg orally once daily with or without food until disease progression or unacceptable toxicity

Clinical Trials

- The FDA approval of Qinlock was based on INVICTUS, a Phase 3 randomized, double-blind, placebo-controlled, international, multicenter clinical study evaluating the safety, tolerability, and efficacy of Qinlock compared to placebo in patients with advanced GIST whose previous therapies have included imatinib, sunitinib, and regorafenib.
- Patients were randomized 2:1 to either 150 mg of Qinlock or placebo once daily.
- The primary efficacy endpoint was progression-free survival (PFS) as determined by independent radiologic review using modified Response Evaluation Criteria in Solid Tumors (RECIST).
- The median PFS in the study was 6.3 months compared to 1.0 month in the placebo arm and significantly reduced the risk of disease progression or death by 85% ($p<0.0001$).
- Secondary endpoints as determined by independent radiologic review using modified RECIST include Objective Response Rate (ORR) and Overall Survival (OS).
- Qinlock demonstrated an ORR of 9.4% compared with 0% for placebo ($p = 0.0504$).
- Qinlock also demonstrated a median OS of 15.1 months compared to 6.6 months in the placebo arm and reduced the risk of death by 64%.

Inqovi (CEDAZURIDINE; DECITABINE)

- FDA approved 7/7/20
- INQOVI is a combination of decitabine, a nucleoside metabolic inhibitor, and cedazuridine, a cytidine deaminase inhibitor, indicated for treatment of adult patients with myelodysplastic syndromes (MDS), including previously treated and untreated, de novo and secondary MDS with the following FrenchAmerican-British subtypes (refractory anemia, refractory anemia with ringed sideroblasts, refractory anemia with excess blasts, and chronic myelomonocytic leukemia [CMML]) and intermediate-1, intermediate-2, and high-risk International Prognostic Scoring System groups. Inqovi is supplied as a tablet for oral administration.
- The recommended dosage of Inqovi is 1 tablet (35 mg decitabine and 100 mg cedazuridine) taken orally once daily on Days 1 through 5 of each 28-day cycle. Take Inqovi on an empty stomach.

Clinical Trials

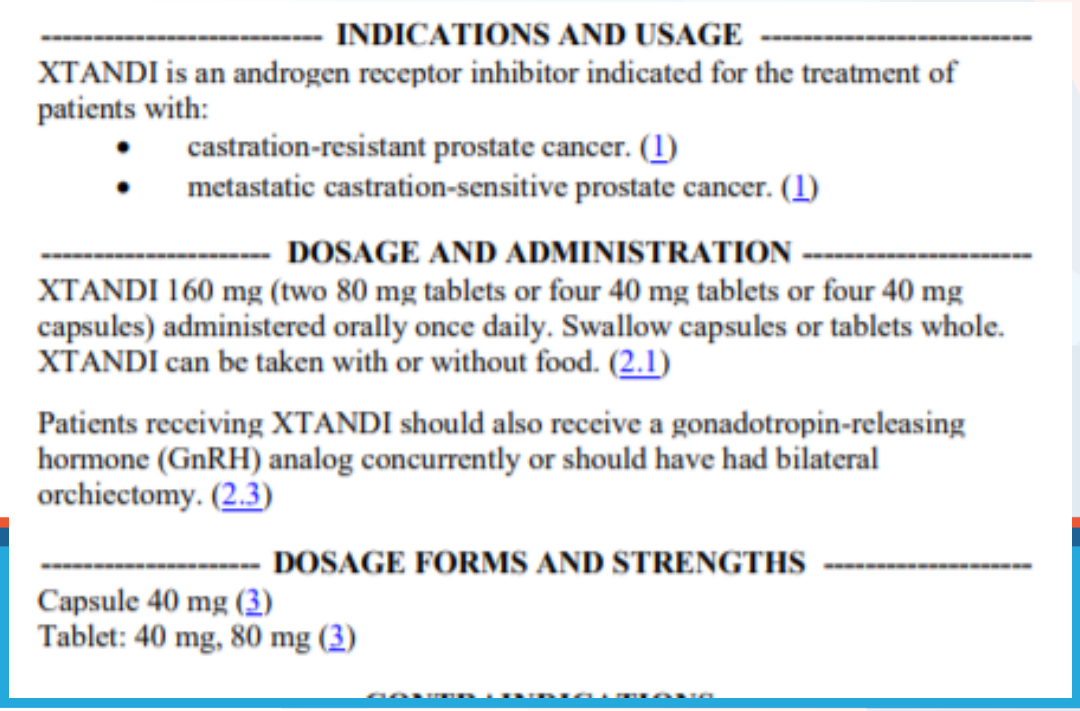
- The FDA approval of Inqovi was based on results of two randomized, open-label crossover trials.
- The ASTX727-01-B trial included 80 adults with myelodysplastic syndrome (IPPS intermediate-1, intermediate-2 or high risk) or CMML. The ASTX727-02 trial included 133 adults with myelodysplastic syndrome or CMML, including those with all French-American-British classification criteria and IPSS prognostic scores.
- Patients in both trials were randomly assigned to 35 mg decitabine and 100 mg cedazuridine orally, then decitabine dosed at 20 mg/m2 IV in the second cycle.
- Both treatments were administered once daily on days 1 through 5 of 28-day cycles. The other half of patients received the reverse sequence. Starting with the third cycle, all patients received decitabine and cedazuridine orally once daily on days 1 through 5 of each 28-day cycle. Treatment continued until unacceptable toxicity or disease progression.
- Results of both trials showed similar drug concentrations between the oral combination of decitabine and cedazuridine and IV decitabine.
- Approximately half of the patients who had been dependent on transfusions no longer required red blood cell or platelet transfusions during any consecutive 8-week post-baseline period.

Adverse Events

- The most common adverse reactions (≥ 20%) were fatigue, constipation, hemorrhage, myalgia, mucositis, arthralgia, nausea, dyspnea, diarrhea, rash, dizziness, febrile neutropenia, edema, headache, cough, decreased appetite, upper respiratory tract infection, pneumonia, and transaminase increased.
- The most common Grade 3 or 4 laboratory abnormalities (≥ 50%) were leukocytes decreased, platelet count decreased, neutrophil count decreased, and hemoglobin decreased.

Xtandi (enzalutamide)

- FDA approval of tablet formulation on 8/4/20 (approved in Japan 3/1/18)
- Both the 40 mg XTANDI Tablets and 80 mg XTANDI Tablets are smaller in size than the 40 mg XTANDI Capsules; thus offering a more patient-friendly medication. With the 80 mg tablets, the number of tablets taken each time will also be reduced



INDICATIONS AND USAGE

XTANDI is an androgen receptor inhibitor indicated for the treatment of patients with:

- castration-resistant prostate cancer. (1)
- metastatic castration-sensitive prostate cancer. (1)

DOSAGE AND ADMINISTRATION

XTANDI 160 mg (two 80 mg tablets or four 40 mg tablets or four 40 mg capsules) administered orally once daily. Swallow capsules or tablets whole. XTANDI can be taken with or without food. (2.1)

Patients receiving XTANDI should also receive a gonadotropin-releasing hormone (GnRH) analog concurrently or should have had bilateral orchiectomy. (2.3)

DOSAGE FORMS AND STRENGTHS

Capsule 40 mg (3)
Tablet: 40 mg, 80 mg (3)

Onureg (azacitadine)

- FDA Approved 9/1/20
- ONUREG is a nucleoside metabolic inhibitor indicated for continued treatment of adult patients with acute myeloid leukemia who achieved first complete remission (CR) or complete remission with incomplete blood count recovery (CRi) following intensive induction chemotherapy and are not able to complete intensive curative therapy
- Onureg is available as a 200 & 300mg tablet. The recommended Onureg dose is 300 mg orally once daily with or without food on days 1 through 14 of each 28-day cycle. Continue Onureg until disease progression or unacceptable toxicity.

Clinical Trials

- Efficacy was investigated in QUAZAR (NCT01757535), a multicenter, randomized, double-blind, placebo-controlled trial. Patients (n=472) who achieved CR or CRi with intensive induction chemotherapy with or without receiving subsequent consolidation therapy were randomized 1:1 to receive Onureg 300 mg (n=238) or placebo (n=234) orally on days 1 to 14 of each 28-day cycle.
- The main efficacy outcome measure was overall survival (OS). Median OS was 24.7 months (95% CI: 18.7, 30.5) in the Onureg arm and 14.8 months (95% CI: 11.7, 17.6) in the placebo arm (HR 0.69; 95% CI: 0.55, 0.86; p=0.0009). A subgroup analysis showed consistency in the OS benefit for patients in either CR or CRi.

Adverse Events

Adverse reactions in ≥ 10% patients receiving Onureg were nausea, vomiting, diarrhea, fatigue/asthenia, constipation, pneumonia, abdominal pain, arthralgia, decreased appetite, febrile neutropenia, dizziness, and pain in extremity.

Gavreto (pralsetinib)

- FDA Approved 9/4/20
- GAVRETO is a kinase inhibitor indicated for the treatment of adult patients with metastatic rearranged during transfection (RET) fusion- positive non-small cell lung cancer (NSCLC) as detected by an FDA approved test.
- Gavreto is available as a 100mg capsule. The recommended dosage in adults is 400 mg orally once daily on an empty stomach (no food intake for at least 2 hours before and at least 1 hour after taking GAVRETO)

Clinical Trials

- The efficacy of GAVRETO was evaluated in patients with RET fusion-positive metastatic NSCLC in a multicenter, non-randomized, open-label, multi-cohort clinical trial (ARROW, NCT03037385).
- The study enrolled, in separate cohorts, patients with metastatic RET fusion positive NSCLC who had progressed on platinum-based chemotherapy and treatment-naïve patients with metastatic NSCLC.
- Identification of a RET gene fusion was determined by local laboratories using next generation sequencing (NGS), fluorescence in situ hybridization (FISH), and other tests.
- Among the 114 patients in the efficacy population(s) described in this section, samples from 59% of patients were retrospectively tested with the Life Technologies Corporation Oncomine Dx Target Test (ODxTT).
- Patients with asymptomatic central nervous system (CNS) metastases, including patients with stable or decreasing steroid use within 2 weeks prior to study entry, were enrolled.
- Patients received GAVRETO 400mg orally once daily until disease progression or unacceptable toxicity.

Clinical Trials (cont'd)

Table 6: Efficacy Results in ARROW (Metastatic *RET* Fusion-Positive NSCLC Previously Treated with Platinum Chemotherapy)

Efficacy Parameter	**GAVRETO (N=87)**
Overall Response Rate (ORR)[a] (95% CI)	57 (46, 68)
Complete Response, %	5.7
Partial Response, %	52
Duration of Response (DOR)	(N=50)
Median, months(95%CI)	NE (15.2-NE)
Patients with DOR ≥ 6-months[b], %	80

NE = not estimable
a Confirmed overall response rate assessed by BICR
b Calculated using the proportion of responders with an observed duration of response at least 6 months or greater

Table 7: Efficacy Results for ARROW (Treatment-Naïve Metastatic *RET* Fusion-Positive NSCLC

Efficacy Parameter	**GAVRETO (N=27)**
Overall Response Rate (ORR)[a] (95% CI)	70 (50, 86)
Complete Response, %	11
Partial Response, %	59
Duration of Response (DOR)	**(N=19)**
Median, months (95% CI)	9.0 (6.3, NE)
Patients with DOR ≥ 6-months[b], %	58

NE = not estimable
a Confirmed overall response rate assessed by BICR
b Calculated using the proportion of responders with an observed duration of response at least 6 months or greater

Adverse Events

The most common adverse reactions (≥25%) were fatigue, constipation, musculoskeletal pain, and hypertension.

The most common Grade 3-4 laboratory abnormalities (≥2 %) were decreased lymphocytes, decreased neutrophils, decreased phosphate, decreased hemoglobin, decreased sodium, decreased calcium (corrected), and increased alanine aminotransferase (ALT).

Biosimilar approvals in 2020

Hulio (adalimumab-fkjp)

- Humira (adalimumab)
- FDA Approved 7/2020

Nyvepria (pegfilgrastim-apgf)

- Neulasta (pegfilgrastim)
- FDA Approved 6/2020

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Thank You!

Thanks to all at NCODA for the opportunity to present