Treatment of Advanced NSCLC

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Disclosures

- *ACCC*
- *No conflict of interest*

Unresectable/Advanced NSCLC

- Palliative cytotoxic chemotherapy in PS 0-2:
  - Improves QOL
  - Improves median overall survival and 1-year survival rate
  - Reduces disease-related symptoms
  - Is cost-effective

- PS 3-4: No benefit from cytotoxic chemotherapy
- Early palliative care: Longer median OS (11.6 vs 8.9 months, p=0.02)

NCCN Guidelines® . V.3.2023, 04/13/2023
Temel JS et al. *N Engl J Med*. 2010; 363: 733-42.

Stage IV NSCLC Treatment Considerations
Evaluation of Pathology

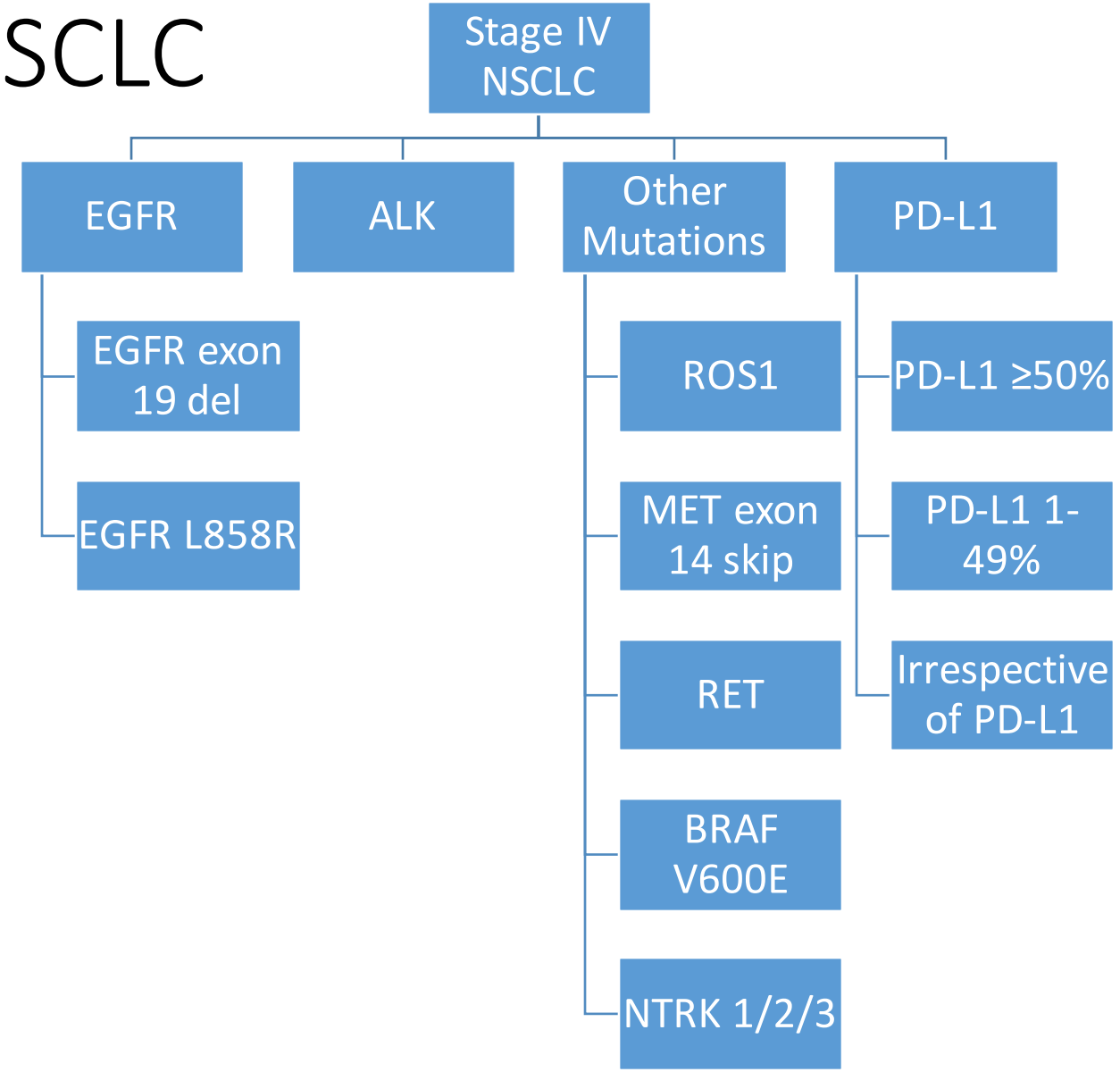
Non-Squamous Histology

- *Recommend* Molecular Testing
  - EGFR (NCCN Cat 1)
  - ALK (NCCN Cat 1)
  - KRAS
  - ROS1
  - BRAF
  - METex14 skipping
  - RET
  - NTRK1/2/3
  - ERBB2 (HER2)
  - *Broad Molecular Profiling*
- PD-L1 Testing (NCCN Cat 1)

Squamous Histology

- *Consider* Molecular Testing
  - EGFR
  - ALK
  - KRAS
  - ROS1
  - BRAF
  - METex14 skipping
  - RET
  - NTRK1/2/3
  - ERBB2 (HER2)
  - *Broad Molecular Profiling*
- PD-L1 Testing (NCCN Cat 1)

Initial Treatment: Advanced NSCLC



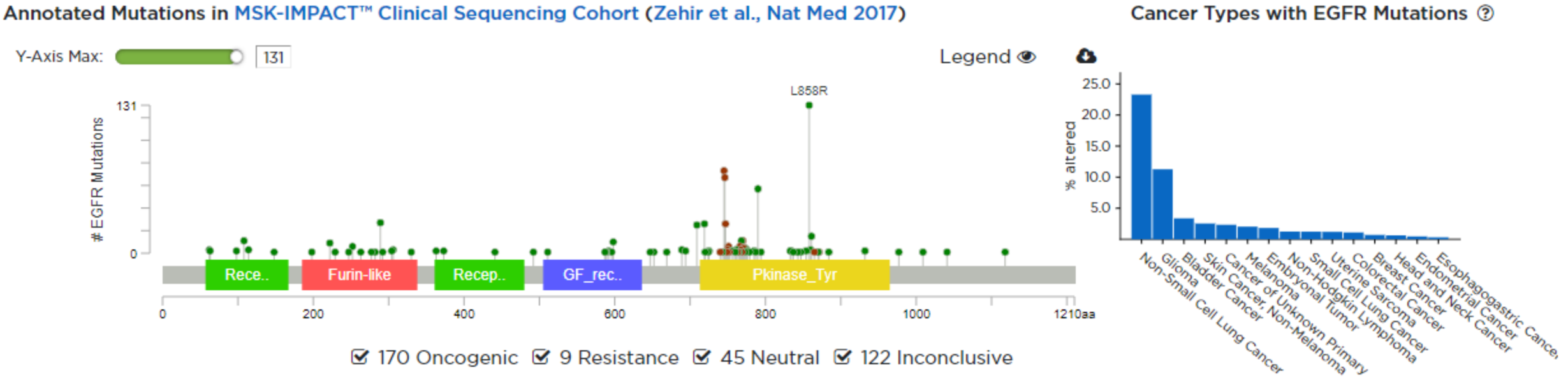
Initial Treatment – Advanced NSCLC

Non-Squamous AND Squamous

- Molecular testing for driver mutation
  - EGFR, ALK, ROS1, BRAF, METex14, RET, NTRK1/2/3
- If molecular testing positive or PD-L1 ≥ 50%, treat with appropriate:
  - Targeted therapy
  - Immune therapy
  - Combination chemotherapy/immune therapy
- If no driver mutation, treat with:
  - Platinum-based doublet ± immune therapy

Actionable Molecular Markers:

EGFR



NCCN Guidelines® . V.3.2023, 04/13/2023
OncoKB™. Chakravarty et al., JCO PO 2017

EGFR Mutation Positive

First Line Therapy

EGFR Inhibitor	Data in First-Line Therapy
Preferred	
Osimertinib 80 mg PO Daily* 3rd gen: ex19del, ex21 L858R, ex21 L861Q, ex18 G719X, ex21 S761I, ex21 T790M	Median PFS osimertinib 18.9 vs 10.2 months with standard EGFR (gefitinib/erlotinib), HR 0.46, 9 = <0.001
Other Recommended	
Erlotinib 150 mg PO Daily* 1st gen: ex19del, ex21 L858R	
Gefinitib 250 mg PO Daily* 1st gen: ex19del, ex21 L858R	
Afatinib 40 mg PO Daily* 2nd gen: ex19del, ex21 L858R, ex21 L861Q, ex18 G719X, ex21 S761I	
Dacomitinib 45 mg PO Daily* 2nd gen: ex19del, ex21 L858R	
Erlotinib 150 mg PO Daily + bevacizumab (15 mg/kg Q 21 Days)	
Erlotinib 150 mg PO Daily + ramucirumab (10 mg/kg Q 21 Days)	

*NCCN® Category 1

NCCN Guidelines® . V.3.2023, 04/13/2023
Soria J-C et al. *N Engl J Med*. 2018; 378: 113-125.

EGFR Mutation Positive

Subsequent Therapy

Previous Therapy	Recommended
Preferred	
Osimertinib	Asymptomatic: local therapy + continue osimertinib Brain only: local therapy + continue osimertinib Symptomatic: local therapy + continue osimertinib *or* systemic therapy
Erlotinib (± bev/ram) Afatinib Gefitinib Dacomitinib	If T790M + : osimertinib If T790M – : local therapy + continue agent *or* systemic therapy

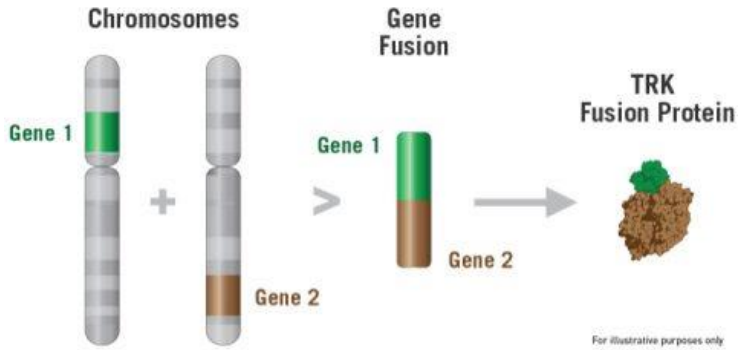
EGFR Exon 20 Insertion Mutation

Recommended	Data
First Line	
Systemic Therapy (Squamous + Non-Squamous)	Median PFS osimertinib 18.9 vs 10.2 months with standard EGFR (gefitinib/erlotinib) HR 0.46, 9 = <0.001
Second Line (After progression on platinum-based chemotherapy ± ICI)	
Amivantamab Titrated dosing weekly x 4, then QOW	CHRYSALIS Trial (phase I dose-escalation/expansion) • ORR 40% • Median DOR 11.1 months • Median PFS 8.3 months • OS 22.8 months Toxicities: • Infusion Reactions (66%), rash (86%), paronychia (45%), musculoskeletal pain, dyspnea, nausea, fatigue, edema, stomatitis, cough, constipation, vomiting
Mobocertinib 160 mg PO Daily	International, non-randomized, open-label phase I/II trial • ORR 28% • Median DOR 17.5 months • Median PFS 7.3 months Toxicities: • Diarrhea, rash, nausea, stomatitis, paronychia • Warnigns: QTc prolongation, interstitial lung disease, cardiac toxicity • Drug interactions: major substrate of CYP3A4, QTc prolongation

NCCN Guidelines® . V.3.2023, 04/13/2023
Park K et al. *J Clin Oncol*. 2021; 39(30): 3391-3402.
Zhou C et al. *JAMA*. 2021; 7(12): e214761.

Actionable Molecular Markers:

ALK Fusion



KEY ✓ Approved in Indication ~ Approved in Other Indication ✕ Lack of Response

Detected Alteration(s) / Biomarker(s)		Associated FDA-approved therapies
NPM1-ALK	Fusion	~ Alectinib, Brigatinib, Ceritinib, Crizotinib, Lorlatinib
CCND1	V209fs	None (VUS)§
ALK-NPM1	Fusion	None (VUS)§

NCCN Guidelines® . V.3.2023, 04/13/2023
https://www.genentechoncology.com/pathways/cancer-tumor-targets/ntrk.html
Guardant 360 Portal

ALK Fusion Positive

First Line Therapy

ALK Inhibitor	Data in First-Line Therapy
Preferred	
Alectinib 600 mg PO BID (2nd generation)	ALEX: Phase III randomized trial, n=303, alectinib vs crizotinib • Investigator-assessed PFS: 34.8 vs 10.9 months • Median OS NR vs 57.4 months • 5-year OS rate of 62.5% vs 45.5%
Brigatinib 90 mg PO Daily x 7 days → 180 mg PO Daily (2nd generation)	ALTA-1L: Phase III randomized, n=275, brigatinib vs crizotinib • 12-month PFS 67% vs 43% • ORR 71% vs 60% • Intracranial response: 78% vs 29%
Lorlatinib 100 mg PO Daily (3rd generation)	CROWN: Phase III randomized, n=296, lorlatinib vs crizotinib • 12-month PFS 78% vs 39% • ORR 76% vs 58% • Intracranial response: 82% vs 23% (72% CR: lorlatinib arm)
Other	
Ceritinib 450 mg PO Daily (2nd generation)	
Crizotinib 250 mg PO BID (1st generation)	

NCCN Guidelines®. V.3.2023, 04/13/2023
Mok T et al. *Ann Oncology*. 2020; 31(8): 1056-1064.
Camidge DR et al. *N Engl J Med*. 2018; 379(21): 2027-2039.
Shaw AT et al. *N Engl J Med*. 2020; 383(21): 2018-2029.

Disease Indication: Lung Adenocarcinoma

Results Summary

IMMUNOTHERAPY MARKERS	GENOMIC ALTERATIONS	
RESULT	**DNA NGS**	**RNA NGS**
Microsatellite Instability Status STABLE | INDETERMINATE | HIGH **Tumor Mutational Burden: 1.6 mut/Mb** LOW | HIGH	• **ALK** p.G1202R	Either extracted nucleic acid was of suboptimal quantity or quality or there was limited tumor tissue available for testing.

Key Comments:

Please note, this specimen is at the borderline for minimal acceptable tumor content for NGS testing.

If PD-L1/other concurrent testing was ordered in conjunction with this test, it will be resulted separately.

Therapeutic Implications

BIOMARKER	VAF %*	TIER	THERAPIES APPROVED THIS INDICATION	THERAPIES APPROVED OTHER INDICATIONS	POSSIBLE THERAPY RESISTANCE	CLINICAL TRIALS
TMB-Low	N/A	2C	None	None	None	None
MSI-Stable	N/A	2C	None	None	None	2 Phase 1/Phase 2 2 Phase 1
ALK p.G1202R (Exon 23)	27	1A	None	Lorlatinib	Alectinib, Brigatinib, Ceritinib, Crizotinib	1 Expanded Access 4 Phase 2 5 Phase 1/Phase 2

*VAF = Variant Allele Frequency. *NOTE: See page 6 for Definitions of Tiers.*

ALK Fusion Positive

Subsequent Therapy

Previous Therapy	Recommended
Preferred	
Crizotinib	Ceritinib Alectinib Brigatinib Lorlatinib
Ceritinib Alectinib Brigatinib	Lorlatinib (including ALK G1202R)

- Caution in discontinuation: flare phenomenon
- Asymptomatic progression: consider local therapy + continuation of current ALK inhibitor

Actionable Molecular Markers:

ROS1 Fusion

ROS1 Fusion Positive

First Line Therapy

ROS1 Inhibitor	Data in First-Line Therapy
Preferred	
Entrectinib 600 mg PO Daily NCCN© 2A Preferred (Targets: TRKA/B/C, ROS1, ALK)	Subgroup Pool Analysis: ALKA, STARTRK-1, and STARTRK-2, n=168 • ORR 68% (CR 6%) • Median DOR: 20.5 months • Median PFS: 15.7 months • Median OS: 47.8 months
Crizotinib 250 mg PO BID NCCN© 2A Preferred (Targets: ALK, HGFR, c-MET, ROS1, RON)	Phase I Expansion Cohort, n=50 • ORR 72% (3 CRs, 33 PRs) • Median DOR: 17.6 months
Other	
Ceritinib 450 mg PO Daily (2nd generation)	

NCCN Guidelines® . V.3.2023, 04/13/2023
Drilon A et al. *Lancet Oncol.* 2020; 12(2): 261-270.
Shaw AT et al. *N Engl J Med. 2014*; 371(21): 1963-1971.

ROS1 Fusion Positive

Subsequent Therapy

Previous Therapy	Recommended
Preferred	
Crizotinib Entrectinib Ceritinib	Lorlatinib NCCN© 2A Preferred Brain Only: Entrectinib (if previously ceritinib/crizotinib)
• Otherwise, consider initial NSCLC systemic treatment options • Asymptomatic progression: consider local therapy + continuation of current ALK inhibitor	

Actionable Molecular Markers:

MET exon 14 skipping

MET exon 14 skipping mutation

First Line Therapy

MET Inhibitor	Data in First-Line Therapy
Preferred	
Capmatinib 400 mg PO BID	GEOMETRY trial: Phase II, multiple-cohort, n=364 • ORR 41% (previously treated cohort), 68% (1st line cohort) • Median PFS: 5.4 months (previously treated), 12.4 (1st line) • Median DOR: 9.7 months (previously treated), 12.6 (1st line) Active patients with brain metastases, n=13 • Intracranial Disease Control: 12 patients • Intracranial Disease Response: 7 patients • Complete response: 4 patients
Tepotinib 450 mg PO Daily	VISION trial: Phase II open-label, n=152 • Overall ORR 56% • Median PFS: 8.5 months • Median DOR: 11.1 months Active patients with brain metastases, n=11 • Intracranial ORR: 55% 12 patients • Median PFS: 10.9 months • Median DOR: 9.5 months
Other	
Crizotinib 250 mg PO BID (1st generation)	

NCCN Guidelines® . V.3.2023, 04/13/2023
Wolf J et al. *N Engl J Med.* 2020; 383(10): 944-957.
Paik PK et al. *N Engl J Med.* 2020; 383(10): 931-943.

MET exon 14 skipping mutation

First Line Therapy

MET Inhibitor	Drug Information
Capmatinib 400 mg PO BID *(with or without food)* Potent, highly selective MET inhibitor, including mutant variants produced by exon 14 skipping	Adverse Effects: • Hepatotoxicity • Interstitial lung disease/pneumonitis, dyspnea • Photosensitivity • Peripheral edema • Nausea/Vomiting • Fatigue • Decreased appetite Drug Interactions: • Major substrate of CYP3A4, moderate inhibitor of CYP1A2
Tepotinib 450 mg PO Daily *(with food)* Selective MET inhibitor, including mutant variants produced by exon 14 skipping	Adverse Effects: • Peripheral edema • Nausea/Vomiting • Fatigue • Decreased appetite • Musculoskeletal pain • Dyspnea Drug Interactions: • Minor substrate of CYP3A4 and P-gp, inhibitor of P-gp

NCCN Guidelines® . V.3.2023, 04/13/2023
Wolf J et al. *N Engl J Med.* 2020; 383(10): 944-957.
Paik PK et al. *N Engl J Med.* 2020; 383(10): 931-943.

Actionable Molecular Markers:

RET Fusion

Results Summary

SNVs/Indels	**ARID1A** G801Vfs*32; **CDKN2A** P114R; **TP53** C277F
Alterations Detected By FISH	**RET Rearrangement:** POSITIVE
Immuno-Oncology Biomarkers	**Microsatellite Instability:** MSI - Stable (MSS); **PD-L1 22C3:** PD-L1 EXPRESSION; **Tumor Mutation Burden:** HIGH
Additional Studies	**HER2 (Other) – with Breast Scoring:** Equivocal; **MET Exon 14 Deletion:** Not Detected; **Pan-TRK:** Not Expressed
Pertinent Negatives	NO alterations detected in the following genes: ALK, BRAF, EGFR, KRAS, MET, ROS1

Interpretation

- High Tumor Mutation Burden (TMB) is an eligibility criterion used for FDA-approved immune checkpoint inhibitor therapy.
- RET rearrangement is associated with response to targeted RET/Pan-TK inhibitor therapies.
- The expression of PD-L1 suggests response to immunotherapy with anti-PD-1 or anti-PD-L1, which are FDA-approved for diverse solid tumor types.

§ See full list of genes tested in Biomarkers Evaluated section at end of report. See Profile Results Detail for Variants of Unknown Clinical Significance.
Abbreviations: SNVs=single nucleotide variants, Indels=insertions/deletions.

RET Fusion Positive

First Line Therapy

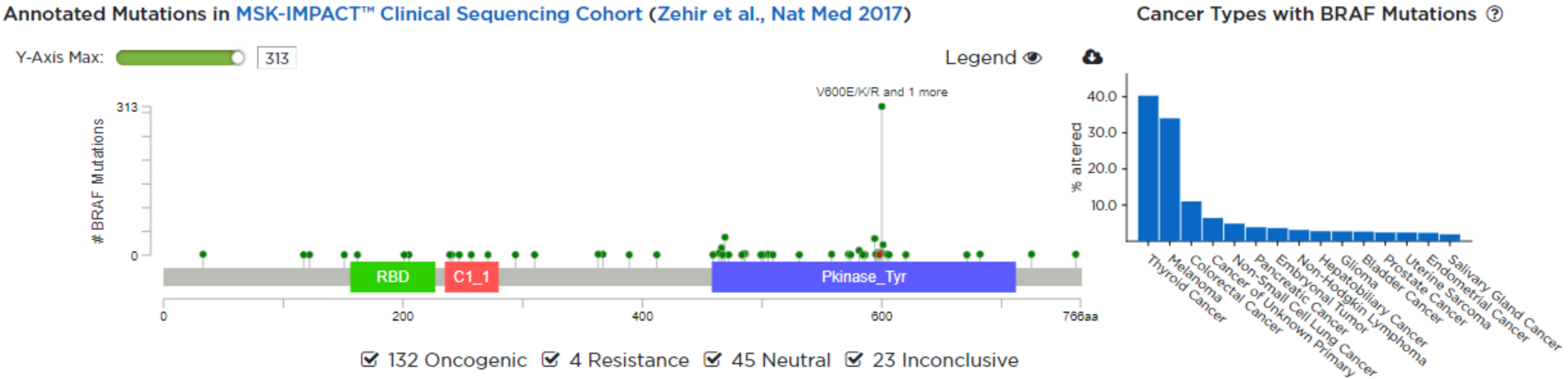
RET Inhibitor	Data in First-Line Therapy
Preferred	
Selpercatinib (NCCN© 2A Preferred) ≥ 50 kg: 160 mg PO BID < 50 kg: 120 mg PO BID Highly selective anti-RET (VEGFR1, VEGFR3, FGFR1/2/3)	Libretto-001: Phase I/II, multiple-cohort • ORR 85% (First line, n=39) • ORR 64% (Second line, n=105) • Median PFS: 18.4 months • Active brain mets (n=11): ORR 91% • Hepatotoxicity, VEGF effects (HTN, wound healing, hemorrhagic risk), hypersensitivity • QTc prolongation, major substrate of CYP3A4, moderate inhibitor of CYP2C8
Pralsetinib (NCCN© 2A Preferred) 450 mg PO Daily Inhibits WT RET, oncogenic RET, and RET mutations	ARROW trial: Phase I/II open-label, n=26 • ORR 73% (First line, n=26) • ORR 61% (Second line, n=80) • Hepatotoxicity, HTN, interstitial lung disease/pneumonitis, hemorrhagic events • Major substrate of CYP3A4
Other	
Cabozantinib 60 mg PO Daily	

NCCN Guidelines®. V.3.2023, 04/13/2023
Drilon A et al. *N Engl J Med. 2020*; 383(9): 813-824.
Gainor JF et al. *J Clin Oncol*. 2020; 38(15_supp): 9515.

Actionable Molecular Markers:

BRAF V600E

Detected Alteration(s) / Biomarker(s)		Associated FDA-approved therapies
BRAF	V600E	Dabrafenib+trametinib Binimetinib, Cobimetinib, Dabrafenib, E
TP53	Y234C	None
EGFR	L372L	Synonymous Alteration§
ARAF	P216R	None (VUS)§



BRAF V600E/K/D mutation

First Line Therapy

BRAF/MEK Inhibitor	Data in First-Line Therapy
Preferred	
Dabrafenib 150 mg PO BID BRAF inhibitor Trametinib 2 mg PO Daily MEK inhibitor	Phase II open-label, multiple cohort, n = 57 pre-treated/36 treatment-naïve • ORR 68.4% (pre-treated), 63.9% (treatment-naïve) • Median PFS 10.2 months and 10.8 months, respectively • Median OS 18.2 months and 17.3 months, respectively • Dermatologic toxicity, drug fever, cardiotoxicity, G6PD hemolytic anemia, ophthalmologic toxicity, interstitial lung disease/pneumonitis, secondary malignancy • QTc prolongation
Other	
Vemurafenib 960 mg PO BID Dabrafenib 150 mg PO BID	

NCCN Guidelines® . V.3.2023, 04/13/2023
Planchard D et al. *J Thorac Oncol*. 2022; 17(1): 103-115.

Actionable Molecular Markers:

NTRK 1/2/3 Fusion

NTRK 1/2/3 Fusion Positive

First Line Therapy

NTRK Inhibitor	Data in First-Line Therapy
Preferred	
Larotrectinib 100 mg PO BID	Phase I/II trial multiple tumor types, n=55 • ORR 75-80% (CR 6%) • 1 year DOR: 71% • 1 year PFS: 55% • Toxicites: nervous system disorders, arthralgia/myalgia
Entrectinib 600 mg PO Daily	Subgroup Pool Analysis: ALKA, STARTRK-1, and STARTRK-2, n=54 [10 tumor types, 19 histologies] • ORR 57% (CR 7%) • Median DOR: 10 months • Toxicites: weight gain, anemia, nervous system disorders, cardiotoxicity • QTc prolongation
Other	
Consider initial NSCLC systemic treatment options	

NCCN Guidelines®. V.3.2023, 04/13/2023
Drilon A et al. *N Engl J Med.* 2018; 378(8): 731-739.
Doebele RC et al. *Lancet Oncol.* 2020; 21(2): 271-282.

No Actionable Mutations

(First Line Setting)

Non-Squamous NSCLC
(No actionable molecular markers)

PD-L1 Status	1st Line Treatment Options (NCCN® Category 1 Unless Otherwise Noted)
PD-L1 ≥ 50%	Pembrolizumab[P] Atezolizumab[P] Cemiplimab[P] (Carboplatin or cisplatin) + pemetrexed + pembrolizumab[P]*
PD-L1 1-49%	Pembrolizumab (NCCN® Category 2B, useful in certain circumstances)
Irrespective of PD-L1 Status	<u>Immunotherapy Candidate:</u> (Carboplatin or cisplatin) + pemetrexed + pembrolizumab[P]* Carboplatin + paclitaxel + bevacizumab + atezolizumab[o] Carboplatin + nab-paclitaxel + atezolizumab[o] Nivolumab + ipilimumab + pemetrexed + (cisplatin or carboplatin)[o] Nivolumab + ipilimumab[o] Cemipilimab + (pemetrexed or paclitaxel) + (cisplatin or carboplatin)[o] Tremelimumab + durvalumab + carboplatin + nab-paclitaxel[o] Tremelimumab + durvalumab + (cisplatin or carboplatin) + pemetrexed <u>Contraindications to Immunotherapy:</u> (Cisplatin or carboplatin) + pemetrexed ± bevacizumab (Cisplatin or carboplatin) + paclitaxel ± bevacizumab Carboplatin + nab-paclitaxel

[P]NCCN® Category 1 Preferred
[o]NCCN® Category 1 Other

Squamous NSCLC

(No actionable molecular markers)

PD-L1 Status	1st Line Treatment Options
PD-L1 ≥ 50%	Pembrolizumab[P] Atezolizumab[P] Cemiplimab[P] Carboplatin + (paclitaxel or nab-paclitaxel) + pembrolizumab[P]
PD-L1 1-49%	Pembrolizumab (NCCN® Category 2B, useful in certain circumstances)
Irrespective of PD-L1 Status	<u>Immunotherapy Candidate:</u> Carboplatin + (paclitaxel or nab-paclitaxel) + pembrolizumab[P] Nivolumab + ipilimumab + paclitaxel + carboplatin[o] Nivolumab + ipilimumab[o] Cemipilimab + paclitaxel + (cisplatin or carboplatin)[o] Tremelimumab + durvalumab + carboplatin + nab-paclitaxel Tremelimumab + durvalumab + (cisplatin or carboplatin) + gemcitabine <u>Contraindications to Immunotherapy:</u> Carboplatin + nab-paclitaxel Carboplatin + paclitaxel Carboplatin + gemcitabine Carboplatin + docetaxel

[P]NCCN® Category 1 Preferred
[o]NCCN® Category 1 Other

Examples of Platinum-Based Doublets

Non-Squamous

- Cisplatin/Pemetrexed
- Carboplatin/Pemetrexed
- Carboplatin/Paclitaxel
- Carboplatin/nab-paclitaxel
- Bevacizumab/Carboplatin/Paclitaxel
- Bevacizumab/Carboplatin/Pemetrexed
- Bevacizumab/Cisplatin/Pemetrexed
- Carboplatin/Docetaxel
- Carboplatin/Gemcitabine
- Cisplatin/Gemcitabine
- Cisplatin/Docetaxel

Squamous

- Cisplatin/Pemetrexed
- Carboplatin/Paclitaxel
- Carboplatin/nab-paclitaxel
- Carboplatin/Docetaxel
- Carboplatin/Gemcitabine
- Cisplatin/Gemcitabine
- Cisplatin/Docetaxel

- ORR = 14-71%
- No doublet superior
- Histology drives preference

NCCN Guidelines® . V.3.2023, 04/13/2023

Maintenance Therapy

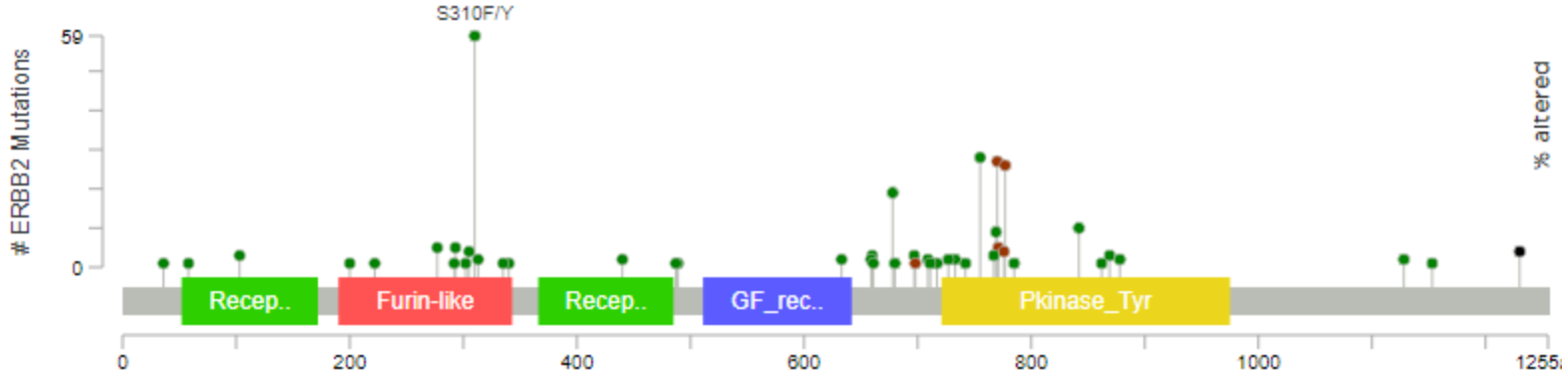
- Continuation of at least one agent, to progression or poor tolerability
- After 4-6 cycles of chemotherapy combination (without progression)
- Agents:
  - Atezolizumab
  - Pembrolizumab
  - Bevacizumab
  - Pemetrexed
  - Ipilimumab/nivolumab
  - Cemiplimab
  - Durvalumab

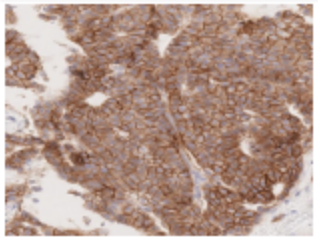
Subsequent Therapy

Actionable Molecular Target

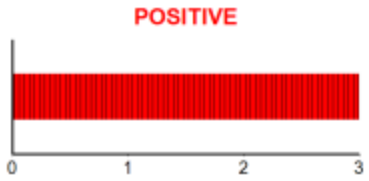
Subsequent Targeted Therapy:

ERBB2 (HER2) mutation





HER2 Breast: POSITIVE
Score: 3+
Percentage of Cells with Uniform Intense Complete Membrane Staining: **40%**



Reference Ranges	
Positive	**3+**
Equivocal/Low *	**2+**
Negative/Low *	**1+**
Negative	**0**

Detected Alteration(s) / Biomarker(s)

ERBB2	A775_G776insYVMA (Exon 20 insertion)
NTRK3	R678*
VHL	S68L

ERBB2 (HER2) mutation

→ After progressing on prior platinum-based therapy

Treatment	Data
Preferred	
Fam-trastuzumab deruxtecan 5.4 mg/kg IV Q 21 Days	Phase II mulitcenter, randomized, blinded, dose-optimization trial, n=91 • ORR 55% • Median DOR 9.3 months • Median PFS 8.2 months • Median OS 17.8 months • Cardiotoxicity, interstitial lung disease/pneumonitis
Other	
Ado-trastuzumab emtansine 3.6 mg/kg IV Q 21 Days	

NCCN Guidelines® . V.3.2023, 04/13/2023
Li BT et al. *New Engl J Med.* 2022; 386(3): 241-251.
Li BT et al. *J Clin Oncol.* 2018; 36(24): 2532-2537.

Subsequent Targeted Therapy:

KRAS G12C

KEY ✓ Approved in Indication ~ Approved in Other Indication ✗ Lack of Response

Detected Alteration(s) / Biomarker(s)		Associated FDA-approved therapies
KRAS	G12C	~ Binimetinib
TP53	Splice Site SNV	None
AR	E340E	Synonymous Alteration§
FGFR2	N147K	None (VUS)§

KRAS G12C mutation

→ After progressing on prior standard therapy

Treatment	Data
Preferred	
Sotorasib 960 mg PO Daily Irreversibly and covalently binds mutant KRAS at the cysteine through interaction with P2 pocket, locking protein in inactive state	CodeBreak100 Trial: multicenter, single-arm, open-label phase II, n=126 • ORR 37.1% (CR in 3.2%) • Median DOR: 11.1 months • Median PFS: 6.8 months • Median OS: 12.5 months • Hepatotoxicity, diarrhea, interstital lung disease/pneumonitis, arthralgia/myalgia, nausea, fatigue, cough • Major substrate of CYP3A4, moderate inducer of CYP3A4
Adagrasib 450 mg PO Daily Irreversibly and covalently binds mutant KRAS at the cysteine through interaction with P2 pocket, locking protein in inactive state	KRYSTAL-1 trial: Phase I/II open-label, n=116 • ORR 42.9% • Median DOR: 8.5 months • Median PFS: 6.5 months • Median OS: 12.6 months • CNS ORR: 33.3% • Hepatotoxicity, diarrhea, interstital lung disease/pneumonitis, arthralgia/myalgia, nausea, fatigue, cough, neurotoxicity, peripheral edema • QTc prolongation, major substrate of CYP3A4, moderate CYP2D6 inhibitor, strong CYP3A4 inhibitor

NCCN Guidelines® . V.3.2023, 04/13/2023
Skoulidis F et al. *N Engl J Med. 2021.*
Janne PA et al. *N Engl J Med.* 2022; 387(2): 120-131.

Subsequent Therapy
Without Molecular Target

- No previous immunotherapy: (NCCN© Cat 1)
  - Nivolumab
  - Pembrolizumab(PD-L1+ required)
  - Atezolizumab
- No previous immunotherapy OR previous immunotherapy:
  - Pemetrexed (non-squamous only)
  - Docetaxel
  - Gemcitabine
  - Docetaxel + Ramucirumab

NSCLC, Stage IV
Review of Treatment Options

Kelsey Finch, PharmD, BCOP
Clinical Oncology Pharmacist
Columbus Regional Health Cancer Center