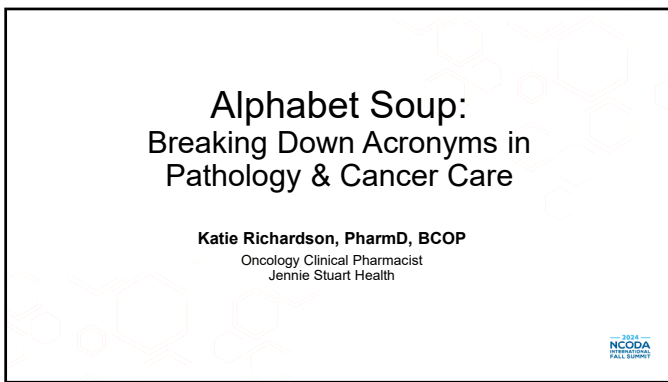
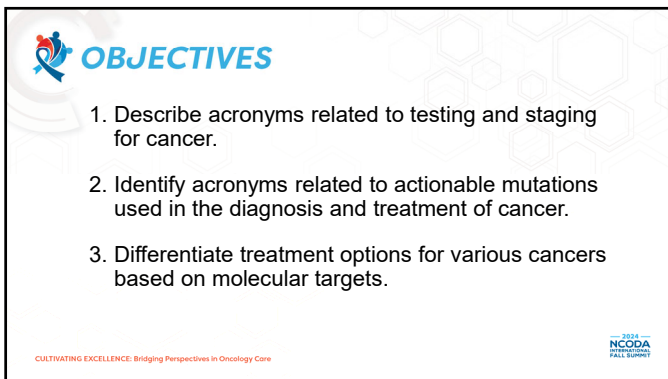





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No relevant financial relationships from the past 24 months have been identified for the following faculty and planners of this CE activity:

- Katie Richardson, PharmD, BCOP
- Mary Anderson, BSN, RN, OCN
- Tahsin Imam, PharmD
- Daisy Doan, PharmD

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Staging/Testing

- TNM (Tumor, Node, Metastasis)
- IHC (Immunohistochemistry)
- FISH (Fluorescence In Situ Hybridization)
- NGS (Next Generation Sequencing)
- ctDNA (circulating tumor DNA)

QNS	Quantity Not Sufficient
Test Not Performed	TNP
VUS	Variant of Unknown Significance

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TNM Staging System

- T - Tumor- describes the size of the tumor and any spread of cancer into nearby tissue
- N - Node- describes spread of cancer to nearby lymph nodes
- M - Metastasis- describes metastasis (spread of cancer to other parts of the body)

Primary tumor (T)
TX: Main tumor cannot be measured
T0: Main tumor cannot be found
T1, T2, T3, T4: Refers to the size and/or extent of the main tumor. The higher the number after the T, the larger the tumor or the more it has grown into nearby tissues. T's may be further divided to provide more detail, such as T3a and T3b.
Regional lymph nodes (N)
NX: Cancer in nearby lymph nodes cannot be measured
N0: There is no cancer in nearby lymph nodes
N1, N2, N3: Refers to the number and location of lymph nodes that contain cancer. The higher the number after the N, the more lymph nodes that contain cancer.
Distant metastasis (M)
MX: Metastasis cannot be measured
M0: Cancer has not spread to other parts of the body
M1: Cancer has spread to other parts of the body

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https://www.cancer.gov/publications/resources/cancer/tnm/staging-system#:~:q=staging-system&context=staging-system Accessed September 30, 2024

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IHC- Immunohistochemistry

Immuno → **Histo** → **Chemistry**

A
B

CULTIVATING EXCELLENCE: Bridging Perspectives in Oncology Care
Author: M. Smith, S. A. Kavanagh, C. Chang, February 14, 2023
https://www.ascp.org/education/cancer-care-education/immunohistochemistry. Accessed September 30, 2024
https://www.ascp.org/education/cancer-care-education/immunohistochemistry/immunohistochemistry. Accessed September 30, 2024

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FISH- Fluorescence In Situ Hybridization

DNA probe exposed to fluoro-label

DNA denatured (unzipped)

Hybridization occurs and DNA is reviewed under microscope

CULTIVATING EXCELLENCE: Bridging Perspectives in Oncology Care
https://www.ascp.org/education/cancer-care-education/fluorescence-in-situ-hybridization. Accessed September 30, 2024

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QUESTION 1

How familiar are you with NGS testing and actionable mutations?

- a. Very familiar - I'm a pro!
- b. Somewhat familiar - I know a little bit...
- c. Not at all - What even is NGS?

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https://www.ascp.org/education/cancer-care-education/next-generation-sequencing. Accessed September 30, 2024

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NGS- Next Generation Sequencing

Cancer Screening **Prognosis & Diagnosis** **Cancer Screening** **Maintenance/Surveillance**

WGS **Whole Genome Sequencing**

Whole Exome Sequencing **WES**

TCGA **The Cancer Genome Atlas**

Early Detection
 • Helps in identifying asymptomatic patients by detecting circulating tumor DNA (ctDNA) in the bloodstream
 • May provide more treatment options in earlier stages of cancer disease

Treatment Selection
 • Helps in the identification of existing/ novel biomarkers for treatment stratification and selection
 • May provide the patient with options to enter a clinical trial

Disease/Response Monitoring
 • Helps in detecting recurrence/ progression and adjust treatment

CULTIVATING EXCELLENCE: Bridging Perspectives in Oncology Care
 Winton T. et al. Value & Outcome Spotlight, 2022, 5:1-18.

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Circulating Tumor DNA (ctDNA)

LB **Liquid Biopsy**

Minimal Residual Disease **MRD**

cfDNA **Circulating Free DNA**

Liquid Biopsy

Sample Analysis
 • Identifying tumor ctDNA
 • Analyze and quantification of ctDNA molecules
 • Analyze and identification of ctDNA methylation patterns

Clinical Application
 • Screening/Prognosis
 • Staging/Prognosis
 • Molecular Profiling/ Treatment Selection
 • Treatment Monitoring
 • Treatment Resistance
 • Early Recurrence Detection

CULTIVATING EXCELLENCE: Bridging Perspectives in Oncology Care
 Bao J et al. Int J Mol Sci, 2023, 24, 13219.

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ctDNA – Serial Monitoring

- Neoadjuvant
 - o Response Monitoring
- Adjuvant
 - o Postsurgical MRD assessment
- Surveillance
 - o Recurrence Monitoring
- Metastatic
 - o Assess treatment response

CULTIVATING EXCELLENCE: Bridging Perspectives in Oncology Care
 Shaw JA et al. JCO Precis Oncol, 2024, 8:e2300456.


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Breast- ER/PR

Results (following ER testing by validated IHC assay)		Interpretation/ Report As:
0% to <1% of nuclei stain		ER-Negative
1% - 100% of nuclei stain	1% - 10% of nuclei stain	ER-low-positive (with recommended comment)
	>10% of nuclei stain	ER-positive

ER: Estrogen Receptor
PR: Progesterone Receptor

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NCCN Breast Cancer Guidelines V.4.2024



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Breast- HER2

HER2 testing by validated IHC assay


Batch controls and on-slide controls show appropriate staining

Circumferential membrane staining that is complete, intense, and in > 10% of tumor cells	Weak to moderate complete membrane staining observed in > 10% of tumor cells	Incomplete membrane staining that is faint/barely perceptible and in > 10% of tumor cells	No staining is observed or Membrane staining that is incomplete and is faint/barely perceptible and in ≤ 10% of tumor cells
IHC 3+ positive	IHC 2+ equivocal	IHC 1+ negative	IHC 0 negative

Must order reflex test (same specimen using ISH) or order a new test (new specimen if available, using IHC or FISH)

HER2: Human Epidermal Growth Factor Receptor 2

CULTIVATING EXCELLENCE: Bridging Perspectives in Oncology Care
Wofford, et al. J Clin Oncol 2018; 36:2105-2122




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Ovarian

Upfront	BRCA Breast Cancer 1/2 gene	HRD Homologous Recombination Deficiency	LOH Loss of heterozygosity
	HER2 Breast Cancer 1/2 gene	MSI Microsatellite Instability	MMR Mismatch Repair
Recurrent	BRAF	FRα (FOLR1)	RET
			TMB Tumor Mutational Burden
			NTRK

CULTIVATING EXCELLENCE: Bridging Perspectives in Oncology Care
NCCN Ovarian Cancer Guidelines V.3.2024
Thomas, et al. J Clin Oncol 2023; 41:2017




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Ovarian- BRCA

- Treatment Considerations
 - Improved response to platinum agents
 - Response to PARP inhibitors
- Prognosis
 - Positive survival benefit
- Genetics
 - Risk of other malignancies (breast, pancreatic, prostate, melanoma)
 - Family Members

CULTIVATING EXCELLENCE: Bridging Perspectives in Oncology Care
Nehf RT, et al. The Adv Med Oncol. 2017.

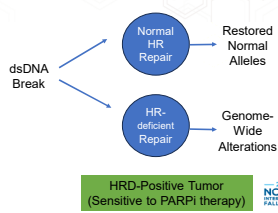


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HRD- Homologous Recombination Deficiency


- Treatment Considerations
 - Magnitude of benefit of PARPi in patients without BRCA
- Prognosis
 - Positive survival benefit
- Genetics
 - HRD present in 50% of ovarian cancers
 - Half of HRD cases are BRCA+



CULTIVATING EXCELLENCE: Bridging Perspectives in Oncology Care
NCCN Ovarian Cancer Guidelines V.3.2024




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TMB- Tumor Mutation Burden

- Number of mutations in a section of DNA
- Reported as mutations per megabase (mut/Mb)
- Cancers with TMB ≥ 10 mut/Mb may be more likely to respond to immune checkpoint inhibitors

CULTIVATING EXCELLENCE: Bridging Perspectives in Oncology Care
Furco, et al. JAMA Oncology. 2021.



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 **FR α (FOLR1), RET, and NTRK**

- Folate Receptor- α (FOLR1)
 - Mirvetuximab soravtansine-gynx/bevacizumab
- RET
 - Selpercatinib
- NTRK
 - Entrectinib, larotrectinib, repotrectinib

CULTIVATING EXCELLENCE: Bridging Perspectives in Oncology Care
Bak HJ, et al. *Br J Clin Oncol*. 2023
NCCN Ovarian Cancer Guidelines V.3.2024

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 **QUESTION 2**


Are you aware that some mutations provide information on what drugs NOT to use?

- a. Yes - I absolutely knew that!
- b. No - That's new information to me!
- c. Unsure - I still don't know what's going on

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 **Colon**


- RAS
 - KRAS
 - NRAS (Neuroblastoma RAS)
- BRAF
- MMR/MSI
- HER2

LS	Lynch Syndrome
Wild Type	WT
FAP	Familial adenomatous polyposis

CULTIVATING EXCELLENCE: Bridging Perspectives in Oncology Care
NCCN Colon Cancer Guidelines V.9.2024

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Colon- RAS

- KRAS mutated in ~40% cases
- NRAS mutated in 3-5% cases
- Patients with RAS mutations should not be treated with cetuximab or panitumumab

CULTIVATING EXCELLENCE: Bridging Perspectives in Oncology Care
NCCN Colon Cancer Guidelines, V.9.2024




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Colon- BRAF

- BRAF-V600E mutated in 8-12% cases
 - Associated with poor response to standard chemo and shorter overall survival
 - ~30% also have microsatellite instability
- BRAF inhibition requires EGFR inhibitor combination for efficacy

CULTIVATING EXCELLENCE: Bridging Perspectives in Oncology Care
Tabernero J, et al. ASCO Educational Book. 2022




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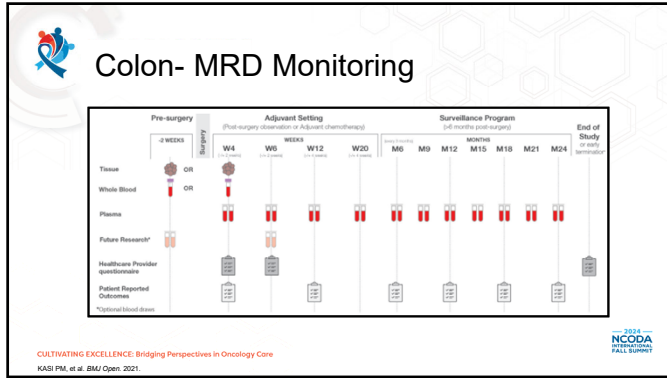
Colon- MMR/MSI

- **Microsatellite Instability**
 - MSS- Microsatellite stable
 - MSI-H- Microsatellite instability- high
 - MSI-L- Microsatellite instability- low
- **Mismatch Repair**
 - dMMR- deficient mismatch repair
 - pMMR- proficient mismatch repair

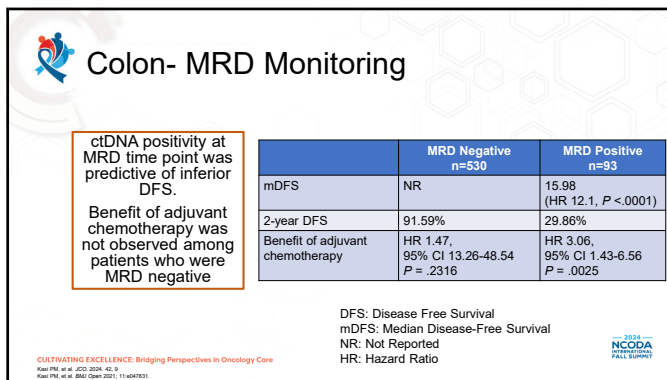
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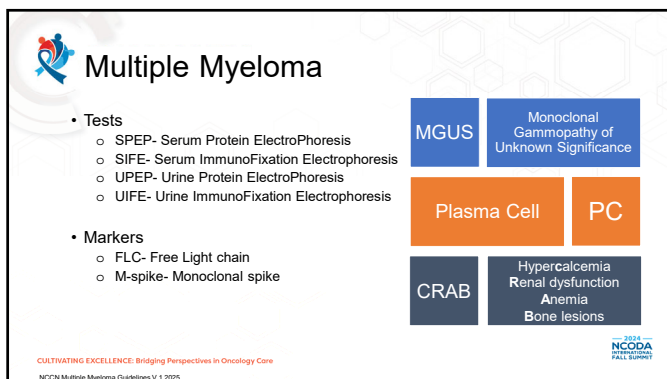
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Multiple Myeloma- M Spike

- Gamma globulin region of SPEP/UPEP
 - Sharp spike (M component)
- Reflex IFE
 - Determines which M component is elevated
 - Kappa (κ)
 - Lambda (λ)

CULTIVATING EXCELLENCE: Bridging Perspectives in Oncology Care
www.Myeloma.org/monoclonal-protein-test/ Accessed September 30, 2024

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Final Thoughts- Resources

- NCCN Guidelines- Abbreviations page
- Professional Organizations
 - ESMO. <https://oncologypro.esmo.org/education-library/medical-abbreviations> Accessed October 1, 2024.
 - ONS. <https://www.ons.org/clinical-practice-resources/ons-biomarker-database> Accessed October 1, 2024.
- Educational Websites
 - <https://www.knowyourbiomarker.org/>

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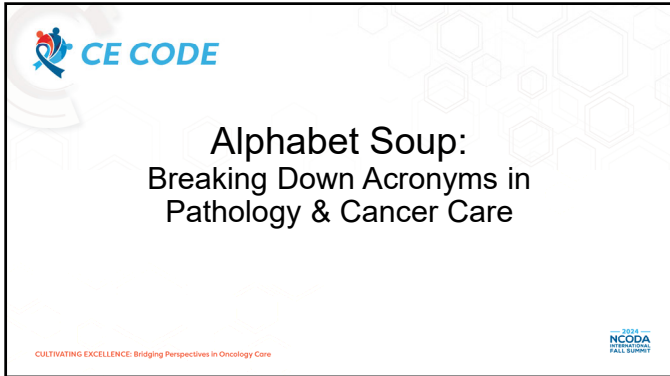
QUESTION & ANSWERS

**Alphabet Soup:
Breaking Down Acronyms in
Pathology & Cancer Care**

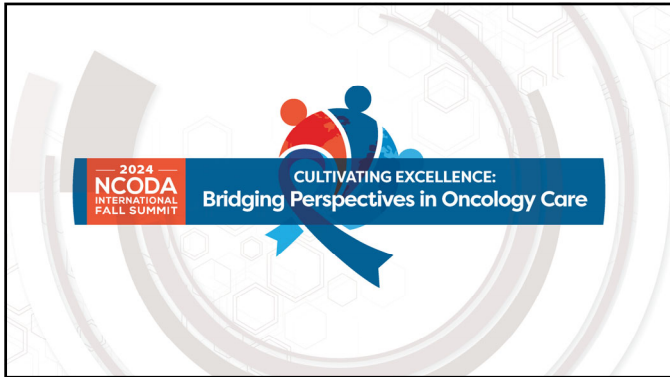
Katie Richardson, PharmD, BCOP
Oncology Clinical Pharmacist
Jennie Stuart Health

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