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Title

An Integrated Multidisciplinary Evaluation Platform and Early Experience for Precision Therapy in Resectable NSCLC

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Authors

Chen, Joy
Toomey, Kyra A
Godoy, Luis A
[et al.](#)

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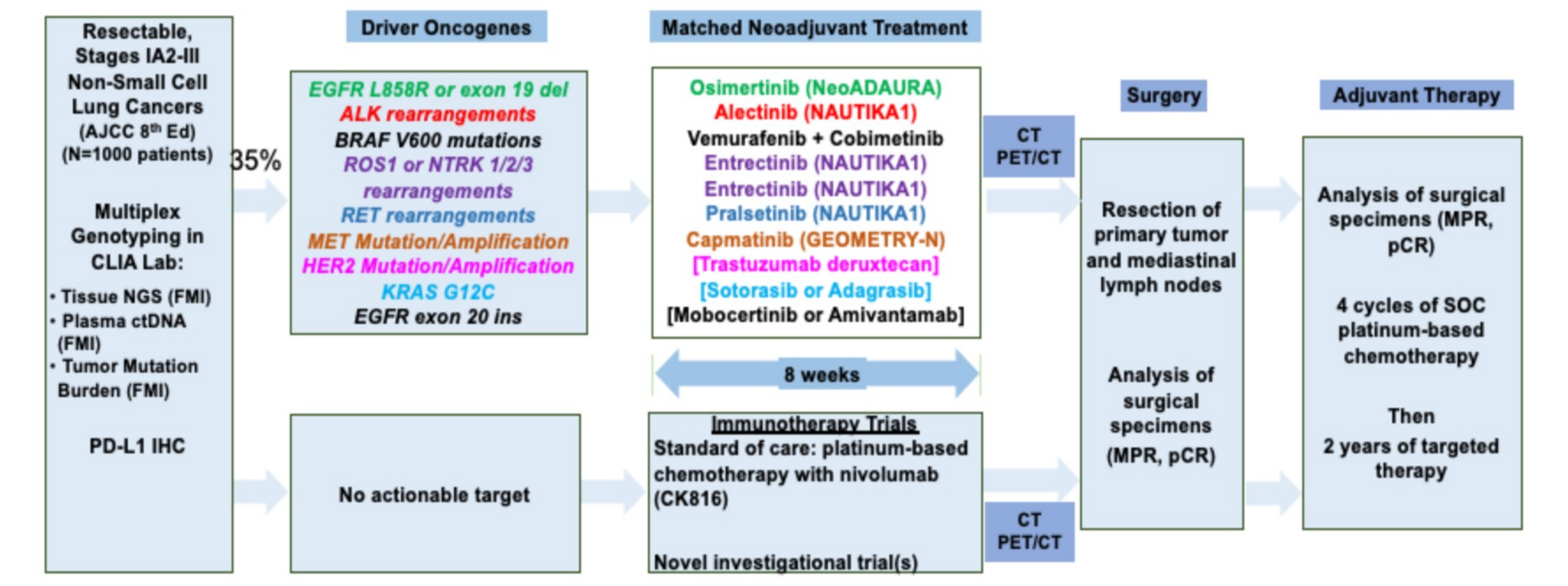
Joy Chen, BS¹, Kyra A. Toomey, BS², Luis A. Godoy, MD³, David Cooke, MD³, Lisa Brown, MD³, Jonathan W. Riess, MD/MS², Cathleen J. Park, MD², Nicholas Stollenwerk⁴, Chinh T. Phan⁴, Danielle L Schneider, CRC⁵, A. Linh Dang-Chu, CCRP⁵, Lorenzo Nardo, MD/PhD⁶, Tianhong Li, MD/PhD^{2,7}

Affiliations: ¹University of California Davis School of Medicine, Sacramento, California, US; ²Division of Hematology/Oncology, Department of Internal Medicine, University of California Davis School of Medicine, University of California Davis Comprehensive Cancer Center, Sacramento, California, US; ³Division of General Thoracic Surgery, Department of Surgery, University of California Davis Health, Sacramento, CA, US; ⁴Division of Pulmonary, Critical Care, and Sleep Medicine, Department of Internal Medicine, University of California Davis School of Medicine, Sacramento, California, US; ⁵Office of Clinical Research, UC Davis Comprehensive Cancer Center, Sacramento, California, US; ⁶Department of Radiology, University of California Davis, Sacramento, CA, US; ⁷Department of Radiology, Interventional Radiology, Veterans Affairs Northern California Health Care System, Mather, California, US

Background

- Lung cancer is the leading cause of cancer related deaths in the United States with 85% of cases classified as non-small cell lung cancer (NSCLC).
- 20-25% of patients with NSCLC present with resectable disease. Despite higher survival rates among patients with resectable NSCLC compared with unresectable or metastatic NSCLC, 30-55% of patients with resectable NSCLC will develop recurrence and die of their disease.
- In December 2020, Osimertinib was approved as adjuvant therapy for EGFR sensitive NSCLC based on the ADAURA trial. There is increasing interest in the clinical efficacy of neoadjuvant molecular targeted therapies for oncogene-drive NSCLC and there are several phase II and phase III trials that are currently evaluating this.
- In March 2022, neoadjuvant nivolumab in conjunction with chemotherapy was approved for Stage IB-IIIa resectable NSCLC based on Checkmate 816. Neoadjuvant immunochemotherapy had significantly longer event-free survival (31.6 versus 20.8 months) and a higher percentage of pathological complete response (24% versus 2.2%) compared with neoadjuvant chemotherapy.
- Clinical application of advancements in standard of care and biomarker guided neoadjuvant therapies for resectable NSCLC are integral in improving clinical outcomes, but this requires a paradigm shift in clinical practice with multidisciplinary collaboration for timely clinical workflow.

Schema for Biomarker-Driven Precision Neoadjuvant Therapy for Stage IA2-III NSCLC

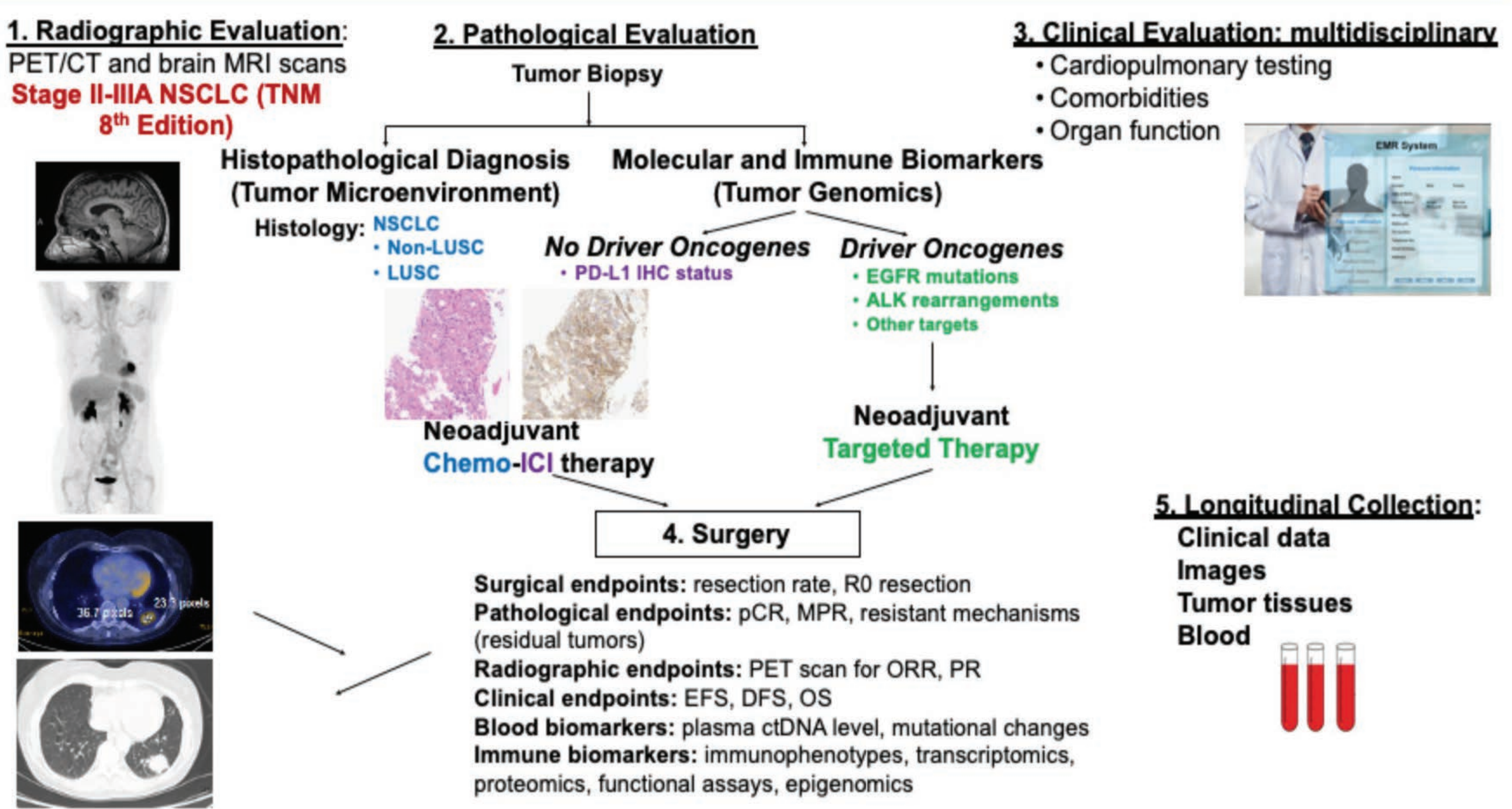


LEADER (LCMC4) (NCT04712877): Neoadjuvant screening trial
 NeoADAURA (NCT04351555): Osimertinib with or without chemotherapy as neoadjuvant therapy for patients With EGFRm positive resectable NSCLC
 NAUTIKA1 (NCT04302025): Phase II neoadjuvant and adjuvant study of multiple therapies in biomarker-selected patients with resectable stages IB-III NSCLC
 GEOMETRY-N (NCT04926831): Phase II neoadjuvant and adjuvant capmatinib in patients with advanced/metastatic MET-dysregulated NSCLC

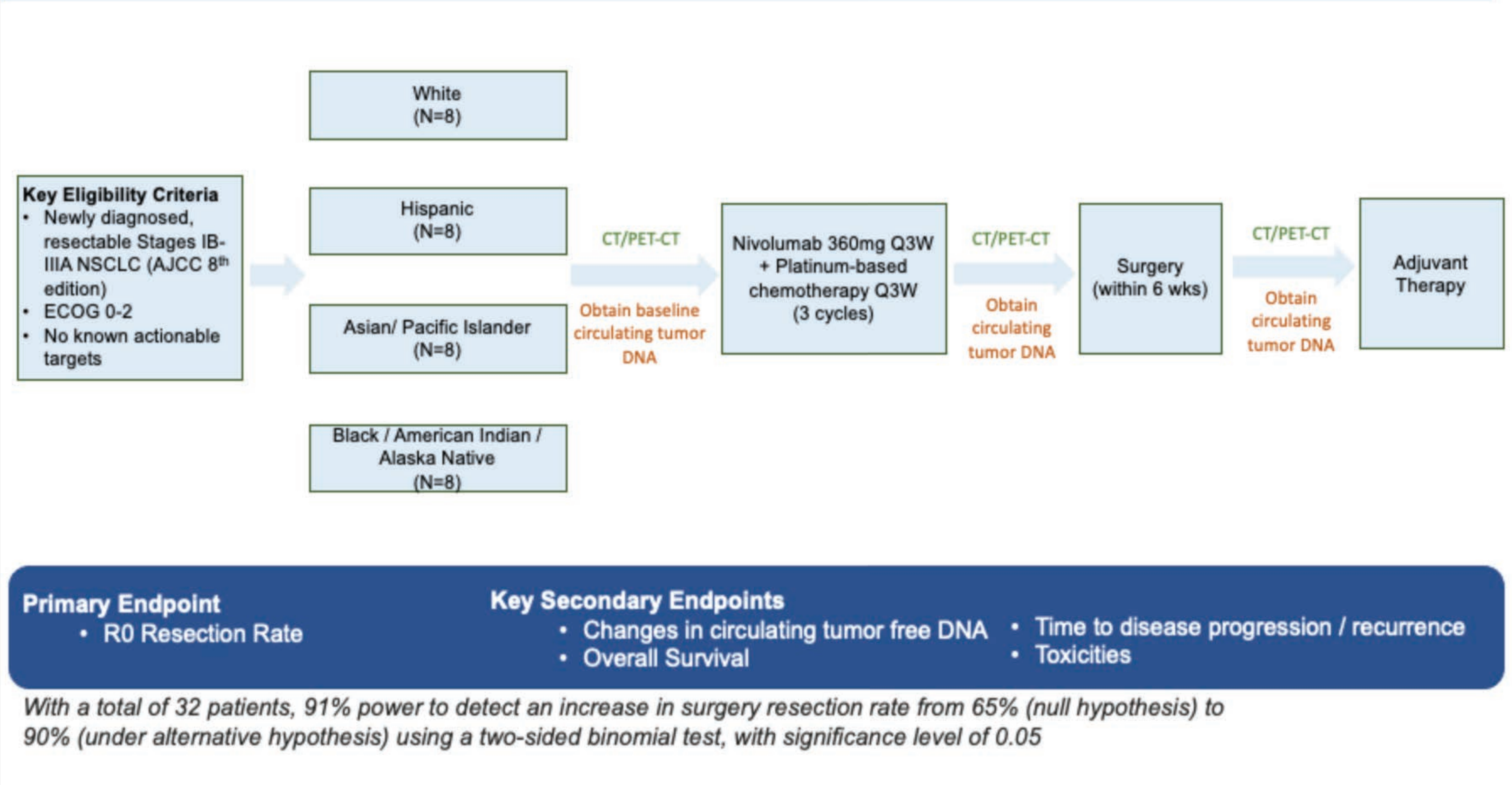
Early-stage NSCLC Patients Screened for Precision Neoadjuvant Therapy

Subject No.	Age	Gender	Race/Ethnicity	Date of lung mass finding	Date of tissue diagnosis	Clinical AJCC Stage	Clinical TNM Stage	Date of molecular testing collection	Date of molecular test result	Start Date of neoadjuvant treatment	Genomic Alterations	PD-L1 IHC or TMB	Neoadjuvant Regimen	End Date of Neoadjuvant Treatment	Date of surgery
1	76	Female	NHW	4/21/22	6/3/22	Stage IIB	cT3N2M0	6/9/22 liquid	6/20/2022 liquid	7/27/22	EGFR E20insertion	5%	CM-816	7/27/22	N/A (Tumor progression)
2	59	Male	NHW	11/23/21	5/19/22	Stage IIB	cT1cN1M0	6/9/22 liquid	6/15/22 liquid	7/6/22	None	1-2%	CM-816	8/23/22	9/22/22
3	65	Male	NHW	3/12/20	6/2/22	Stage IA3	T1cN0M0	N/A (too small)	N/A	N/A	N/A	5%	NA	N/A	9/8/22
4	67	Male	NHW	12/11/20	7/13/22	Stage IA2	T1bNxMx	8/18/22 (Liquid)	8/30/22 (Liquid)	N/A	NF1 splice site	0 Muts/Mb	NA	N/A	9/29/22
5	65	Male	NHW	6/15/22	7/27/22	Stage IIIA	cT4Nx	8/17/22 Liquid	8/27/22 Liquid	10/3/22	PIK3CA H1047R	3 Muts/Mb	CM-816	S/p cycle 1 on 10/3/22	TBD
6	74	Male	NHW	5/13/22	5/26/22	Stage IIIA	T1cN2M0	9/2/22 Tissue	9/14/22 Tissue	N/A	RET fusion	0 Muts/Mb	Pralsetinib	N/A	N/A (Tumor progression)
7	74	Female	NHW	6/7/22	6/28/22	Stage IIIA	cT1cN2	7/14/22 Tissue	8/1/22 Tissue	8/3/22	EGFR L858R	90%	Osimertinib	TBD	TBD
8	78	Female	NHW	5/12/20	7/15/22	Stage IIB	T1bN0M0	7/15/22 Tissue	8/30/22 Tissue	Plan to start on 10/7/22	MET Exon 14 skipping mutation	Not Tested	Capmatinib	TBD	TBD
9	69	Male	NHW	6/17/22	7/15/22	Stage IIIA	T2aN2M0	8/16/22 Tissue	9/6/22 Tissue	Plan to start on 10/7/22	EML4-ALK	50% 2.1 Muts/Mb	Alectinib	TBD	TBD
10	46	Female	Asian	5/24/18	7/27/22	Stage IA3	T1cN0M0	9/2/22 Tissue	9/29/22 Tissue	N/A	EGFR L858R	10%	N/A	NA	Scheduled 10/13
11	72	Female	NHW	7/6/22	8/23/22	Stage IIB	TxN1M0	9/9/22 Tissue	9/26/22 Tissue	2002	KRAS G12S, TERT, SMAD4, RBM10	50% 13.2 Muts/Mb	CM-816 vs atezo+SBRT	TBD	TBD

Schema for Biomarker-Driven Neoadjuvant Treatment for Early-Stage NSCLC



Schema for Neoadjuvant Chemo-immunotherapy Across Different Ethnic/racial Groups



Early-stage NSCLC Patients Screened for Precision Neoadjuvant Therapy

