INTEGRATION OF IMMUNOTHERAPY INTO ADJUVANT THERAPY FOR RESECTED NSCLC: ALCHEMIST CHEMO-IO

Eligibility Criteria (see Section 3.0)

Resected NSCLC enrolled on A151216

NSCLC of any histologic subtype

Stage IB (≥ 4 cm) or stage II-IIIA (per AJCC 7th edition)

Complete R0 resection

ECOG PS 0-1

EGFR and ALK negative locally or centrally on A151216

Candidate for adjuvant platinum-doublet chemotherapy

Eligible for treatment with an immune checkpoint inhibitor

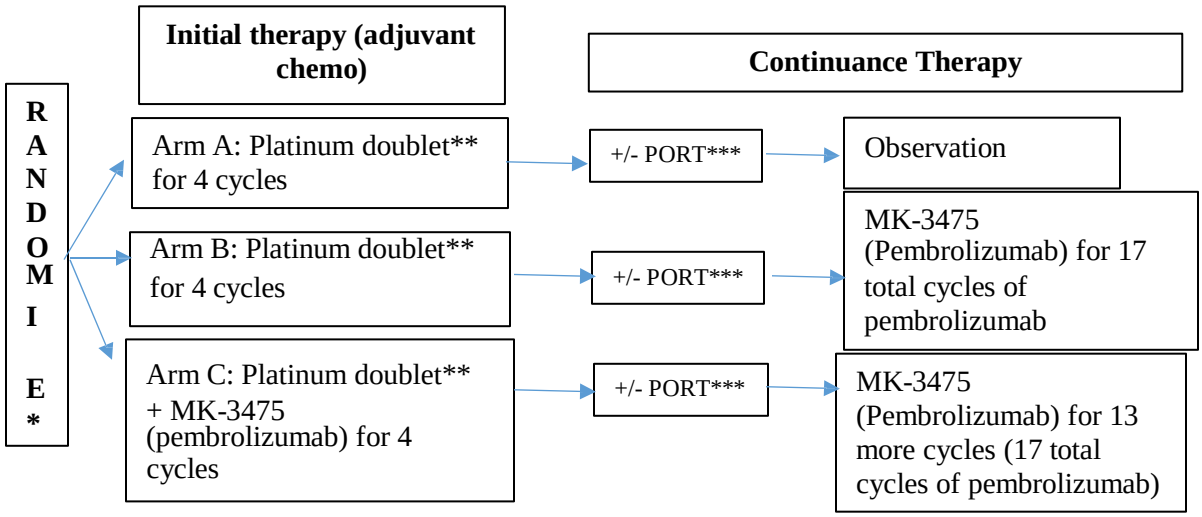
30-77 days post-surgery

Required Initial Laboratory Values

Absolute neutrophil count (ANC): ≥ 1500/mm^3
Platelet count: ≥ 100,000/mm^3
Hemoglobin ≥8 gm/dl
Calc. creatinine clearance: ≥ 45 mL/min
Total bilirubin: ≤ 1.5 x ULN
AST/ALT: ≤ 2.5 x ULN

Please refer to the full protocol text for a complete description of the eligibility criteria and treatment plan.

Schema: 1 cycle = 21 days



* See section 13.4 for further information about the stratification factors and randomization ratio.

** Acceptable regimens include: Cisplatin or carboplatin + pemetrexed; Cisplatin + gemcitabine; Carboplatin + paclitaxel. Treat for up to 4 cycles, as tolerated.

*** Delivery of post-operative radiotherapy (PORT) is at the discretion of the treating physician, see Section 7.3 for further indications. If PORT is recommended for a given patient, the first dose of PORT will be delivered at least 2 weeks and at most 6 weeks following the completion of 4 cycles of chemotherapy +/- MK-3475 (pembrolizumab) AND BEFORE continuing MK-3475 (pembrolizumab) (Arms B or C) or observation (Arm A). PORT Dose: 50-54 Gy in 25-27, 2 Gy daily doses or 28-30, 1.8 Gy daily doses, 5 doses per week. Continuation of MK-3475, if applicable, should occur within 28 days after completion of PORT.

Treatment is to continue until for up to 4 cycles for the patients on observation and for up to 17 weeks for Arms B and C. Patients will be followed for up to 10 years or until death, whichever comes first.

3.1 PATIENT SELECTION

For questions regarding eligibility criteria, see the Study Resources page. Please note that the Study Chair cannot grant waivers to eligibility requirements.

3.2 On-Study Guidelines

This clinical trial can fulfill its objectives only if patients appropriate for this trial are enrolled. All relevant medical and other considerations should be taken into account when deciding whether this protocol is appropriate for a particular patient. Physicians should consider the risks and benefits of any therapy, and therefore only enroll patients for whom this treatment is appropriate.

Physicians should consider whether any of the following may render the patient inappropriate for this protocol:

- Psychiatric illness which would prevent the patient from giving informed consent.
- Medical condition such as uncontrolled infection, uncontrolled diabetes mellitus or cardiac disease which, in the opinion of the treating physician, would make this protocol unreasonably hazardous for the patient.

In addition:

- Women and men of reproductive potential should agree to use an appropriate method of birth control throughout their participation in this study and for 4 months following the end of protocol therapy due to the teratogenic potential of the therapy utilized in this trial. Appropriate methods of birth control include abstinence, oral contraceptives, implantable hormonal contraceptives or double barrier method (diaphragm plus condom).

3.3 Eligibility Criteria

Use the spaces provided to confirm a patient's eligibility by indicating Yes or No as appropriate. It is not required to complete or submit the following page(s).

When calculating days of tests and measurements, the day a test or measurement is done is considered Day 0. Therefore, if a test were done on a Monday, the Monday one week later would be considered Day 7.

A female of childbearing potential is a sexually mature female who: 1) has not undergone a hysterectomy or bilateral oophorectomy; or 2) has not been naturally postmenopausal for at least 12 consecutive months (i.e., has had menses at any time in the preceding 12 consecutive months).

___ **3.2.1 Previously registered to A151216**

___ **3.2.2 Central and/or local testing of EGFR** with no EGFR exon 19 deletion of EGFR L858 R mutation

___ **3.2.3 Central and/or local testing of ALK** with no ALK rearrangement (failed testing is considered negative)

___ **3.2.4 Central and/or local testing of PD-L1 IHC** using one of the following assays: DAKO 22C3, DAKO 28-8, or SP263

Note: Local testing results of EGFR and ALK by a local CLIA certified laboratory is acceptable. The report must indicate the result as well as the CLIA number of the laboratory that performed the assay. Local result of PD-L1 by DAKO 22C3, Dako 28-8, or SP263 are acceptable for enrollment on A081801. Patients with local results for EGFR, ALK and PD-L1 still need to be registered to A151216 and follow all the submissions requirements but do NOT need to wait for the results to proceed to A081801 registration.

___ **3.2.5** Completely resected stage IB (≥ 4 cm), II or IIIA NSCLC with negative margins (complete R0 resection). Patients will be staged according to the 7th edition of the AJCC Cancer Staging Manual, 2010.

Note: Patients with pathologic N2 disease, completely resected, are eligible. However, patients known to have N2 disease prior to surgery are not eligible; guidelines do not recommend up-front surgery for this population.

___ **3.2.6** Complete recovery from surgery. Registration to A081801 must be 30-77 days following surgery.

___ **3.2.7** No prior neoadjuvant or adjuvant therapy for current lung cancer diagnosis.

___ **3.2.8** No prior allogeneic tissue/solid organ transplant

___ **3.2.9** Patients must NOT have uncontrolled intercurrent illness including, but not limited to, serious ongoing or active infection, symptomatic congestive heart failure, uncontrolled cardiac arrhythmia, unstable angina pectoris, that would limit compliance with study requirements.

___ **3.2.10** No current pneumonitis or history of (non-infectious) pneumonitis that required steroids.

___ **3.2.11** HIV-infected patients on effective anti-retroviral therapy with undetectable viral load within 6 months are eligible for this trial.

___ **3.2.12 Age ≥18 years**

___ **3.2.13 ECOG PS: 0-1**

___ **3.2.14** No active auto-immune disease that has required systemic treatment within the last 2 years (e.g., disease-modifying agents, corticosteroids, or immunosuppressive drugs). Replacement therapy (e.g., thyroxine, insulin, or physiologic corticosteroid release therapy for adrenal or pituitary insufficiency) is not considered a form of systemic treatment.

___ **3.2.15 Not pregnant and not nursing,** because this study involves an agent that has known genotoxic, mutagenic and teratogenic effects.

Therefore, for women of childbearing potential only, a negative pregnancy test done ≤ 7 days prior to registration is required.

___ **3.2.16** No patients with a "currently active" second malignancy that is progressing or has required active treatment within the last 3 years. Participants with non-melanoma skin cancers or carcinoma in situ (e.g., breast carcinoma or cervical cancer in situ) that have undergone potentially curative therapy are eligible.

___ **3.2.17** No hypersensitivity (≥ Grade 3) to pembrolizumab and/or any of its excipients

___ **3.2.18** No live vaccine within 30 days prior to registration. Examples of live vaccines include, but are not limited to, the following: measles, mumps, rubella, varicella/zoster (chicken pox), yellow fever, rabies, Bacillus Calmette–Guérin (BCG), and typhoid vaccine. Seasonal influenza vaccines for injection are generally killed virus vaccines and are allowed; however, intranasal influenza vaccines (e.g., FluMist®) are live attenuated vaccines and are not allowed.

___ **3.2.19** No known history of Hepatitis B (defined as HBsAg reactive) or known Hepatitis C virus (defined as HCV RNA [qualitative] is detected) infection.

___ **3.2.20 Required Initial Laboratory Values**

Absolute Neutrophil Count (ANC)	≥ 1,500/mm3
Platelet Count	≥ 100,000/mm3
Hemoglobin	≥8 gm/dl
Calc. Creatinine Clearance	≥ 45 mL/min
Total Bilirubin	≤ 1.5 x upper limit of normal (ULN)
AST / ALT	≤ 2.5 x upper limit of normal (ULN)