1173P - Induction osimertinib in EGFR-mutant stage IIIA/B NSCLC

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Abstract

Background: Definitive chemoradiation (CRT) followed by durvalumab is the standard of care in Stage III NSCLC. Osimertinib showed high efficacy in metastatic and resectable settings and is currently assessed in unresectable IIIA/B. This study aims at testing the efficacy of osimertinib as induction therapy before definitive radiation therapy (RT) in EGFRm stage III patients to induce tumor shrinkage and reduction of the radiation field.

Methods: This phase 2 open-label study enrolled EGFRm NSCLC stage IIIA-C patients. Osimertinib (80 mg) was given daily for a maximum of 12 weeks followed by definitive RT and/or surgery. Response to therapy was assessed by PET-CT at weeks 3, 6, and 12. In case of response, patients were referred to subsequent definitive RT at week 12 while in case of progression, patients were referred to CRT. After RT+/- surgery or CRT, patients were followed (no adjuvant therapy). ORR is the primary endpoint, secondary endpoints are: mPFS, GTV (gross tumor volume) and planned target volume (PTV) before and after treatment. All the patients will be followed for 2 years.

Results: This preliminary analysis includes 13 patients (11 female; age 71.7 ± 6.4 years) with a median follow up of 14.4m (8.1 – 25.9). All non-smokers with adenocarcinoma. 10 patients harbored an exon 19 deletion and 3 had exon 21 L858R mutations. Participants had either stage IIIA (5), IIIB (5), or IIIC (3) disease (Table 1). Among 13 patients who have completed 12 weeks of osimertinib therapy, ORR was 92.3%, (5 CR, 7 PR and 1 PD). Following osimertinib induction, 8 patients completed RT, 3 did not undergo RT (1 not fit, 1 refused and 1 withdrew for unrelated adverse events), 2 underwent surgery with pT1aN0 (1 post-RT & 1 without RT). One patient is undergoing RT. Pre-osimertinib GTV, PTV & V20% were 48.91 cm^3 (13.5 – 143.0), 322.96 cm3 (102 – 929.2) and 38.15% (12.8– 60.3). All variables reduced to 33.5 cm3 (2.99 – 137.7; 31.5% reduction), 202.28 cm^3 (83.4 – 718.1; 37.3% reduction) and 30.73% (18.05 – 44.15; 19.6% reduction), respectively (Table 2). No safety issues reported.

Conclusions: Osimertinib induction in stage III EGFRm NSCLC is feasible and led to tumor shrinkage in 100% of the cases resulting in a significant reduction of the radiation field and enabling preservation of the lung tissue radiation induced toxicity. This chemotherapy-free novel approach should be further investigated as an alternative to CRT in the setting of EGFR-mutations.

Objectives

- Efficacy of osimertinib as induction therapy to reduce tumor size and radiation field in EGFRm stage III patients prior to definitive radiation therapy (RT)

This study was funded by AstraZeneca through an Investigator Initiated Study granted to Prof. Nir Peled.
Helsinki approval: 0431-20-SZMC at Shaare Zedek Medical Center and 0348-17-SOR at Soroka Medical Center.
Dr. Waleed Kian has no disclosures related to this study

Methods

- Phase 2 open-label study enrolled EGFRm NSCLC stage IIIA-C patients.
- Osimertinib (80 mg) daily for 12 weeks → definitive RT (60Gy) and/or surgery.
- PET-CT 6 & 12 wks.
  - Response to treatment → Definitive RT (wk 12)
  - If localized progression → CRT (wk 6 or wk 12)
- Primary endpoint: ORR
- Secondary endpoints: DFS, GTV and PTV (before and after treatment)
- Patient follow-up without adjuvant therapy for 2 yrs

Study Design

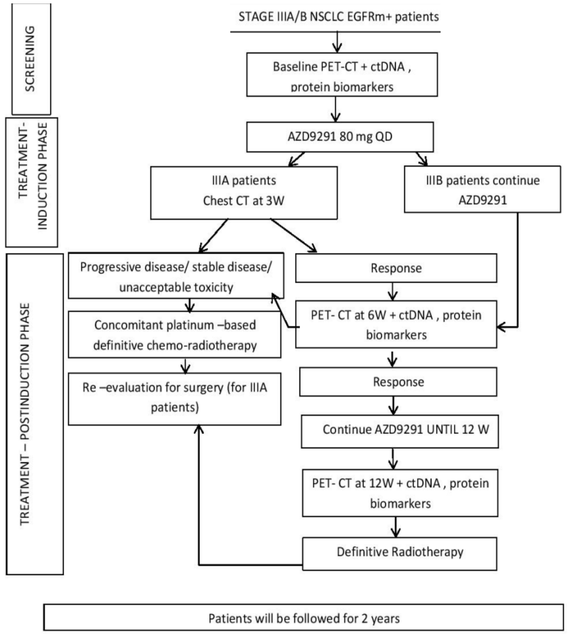

Figure 1. Study Design

Results

- Preliminary analysis of **13** patients w/ median follow-up of 14.4m
- All patients completed 12 wks of osimertinib 80 mg
- **Updated ORR analysis**: 92.3% (5 CR, 7 PR & 1 PD)
- **8 patients completed RT**, 2 patients underwent surgery (pT1aN0), 1 patient currently undergoing RT, 3 patients did not received RT (unfit, refused and withdrew)

Table 1: Demographics

Characteristics	No. of Patients % (N = 13)
Age	
Years	71.7 ± 6.4
Gender	
Male	2 (15)
Female	11 (85)
EGFR-mutation Type	
Exon 19 deletion	10 (77)
Exon 21 L858R	3 (23)
Stage	
IIIA	5 (38.5)
IIIB	5 (38.5)
IIIC	3 (23)

Table 2: Summary of Radiotherapy Response of the 8 Patients that Completed RT

N = 8	Median Pre-Treatment cm^3 (range)	Median Post-Treatment cm^3 (range)	Median reduction % (range)
Gross Tumor Volume (GTV) cm^3	48.9 (13.5 – 143.0)	33.5 (2.99 – 137.7)	39 (4 - 78)
Planned Tumor Volume (PTV) cm^3	323 (102 – 929.2)	202.3 (83.5 – 718.2)	15 (2 — 64)
V20 %	38.2 (12.8– 60.3)	30.7 (-14.5 – 25.8)	19 (-113 — 47)

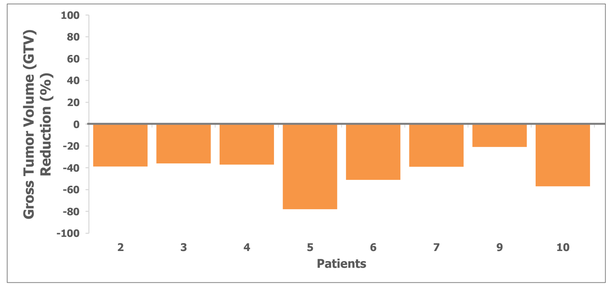

Figure 2. GTV Reduction (%) following osimertinib treatment

Results

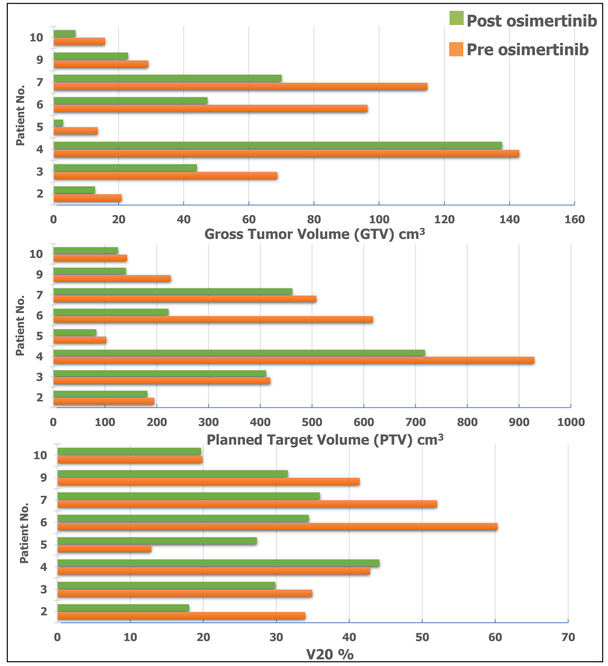

Figure 3. Analysis of 8 patients who completed RT

Conclusions

- Osimertinib induction in stage III EGFRm NSCLC is feasible
- Tumor size reduced in 92.3% of cases
- A median of 39% (range 4% to 78%) reduction in GTV following treatment
- This chemotherapy-free novel approach should be further investigated as an alternative to CRT in the setting of EGFR-mutations

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