

## PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

### ARTICLE DETAILS

#### Title (Provisional)

ASTRUM-LC01 Study Protocol: A Single-arm Phase II Study of Consolidation Serplulimab Following Hypofractionated Radiotherapy with Concurrent Chemotherapy for Patients with Limited Stage Small Cell Lung Cancer

#### Authors

Wu, Yuqi; Deng, Lei; Wang, Jianyang; Zhang, Tao; Cao, Jianzhong; Zhou, Xiaohong; Duan, Jianchun; Bi, Nan

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### VERSION 1 - REVIEW

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<b>Reviewer</b>	<b>1</b>
<b>Name</b>	<b>Coleman, Niamh</b>
<b>Affiliation</b>	<b>Trinity College Dublin, Medical Oncology</b>
<b>Date</b>	<b>03-Jul-2024</b>
<b>COI</b>	<b>NA</b>

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The authors present a well-written investigator-initiated multicenter phase II trial protocol, the ASTRUM-LC01 study, which aimed to investigate the clinical efficacy and safety of serplulimab consolidation therapy after concurrent hypofractionated radiotherapy with chemotherapy in limited-stage small cell lung cancer. The rationale of the study is well-explained, and the merits and limitations are appropriately discussed.

The recent Astrum 005 is the first trial to demonstrate that PD-1 inhibitor plus chemotherapy can also improve OS in ES-SCLC in the first-line, suggesting serplulimab in combination as consolidation may be another valid treatment option for LS-SCLC how have not progressed on primary CRT.

Minor comments:

Introduction – CAPIAN typo, fix to CASPIAN

-any rationale / comment on 1year of therapy (given for eg PD1 inh given as a maximum of 24 months (mo) in ADRIATIC)

Background - ADRIATIC trial is referenced – large phase 3, randomized, double-blind multicenter, global study, assessing durv ± tremelimumab (T) as consolidation tx for pts with LS-SCLC who had not progressed after cCRT.

Recently presented at the annual ASCO meeting by Spigel et al, this should be reported and included if possible given the

- statistically significant and clinically meaningful improvement in OS and PFS compared with placebo in pts with LS-SCLC

- has confirmed consolidation immunotherapy for LS-SCLC – who have not progressed after cCRT...

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<b>Reviewer</b>	<b>2</b>
<b>Name</b>	<b>Yang, Sha</b>
<b>Affiliation</b>	<b>Chengdu University of Traditional Chinese Medicine, Acupuncture and Tuina School/The 3rd Teaching Hospital</b>
<b>Date</b>	<b>11-Jul-2024</b>
<b>COI</b>	<b>NO</b>

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1、 The advantages of Serplulimab combination treatment are not fully explained in the introduction ;

2、 The discussion was too simple and the possible outcomes of the Serplulimab treatment were not discussed.

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<b>Reviewer</b>	<b>3</b>
<b>Name</b>	<b>Li, Jisheng</b>
<b>Affiliation</b>	<b>Qilu Hospital, Cheeloo College of Medicine</b>
<b>Date</b>	<b>04-Aug-2024</b>
<b>COI</b>	<b>None.</b>

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In this clinical trial protocol, the authors designed a prospective multi-center single-arm phase II trial to evaluate the efficacy and safety of chemo-radiotherapy and consolidation with anti-PD-1 antibody serplulimab in LS-SCLC. The study protocol was well organized and clearly presented. Here are some suggestions to be addressed.

1.In the section of “Statistical considerations and analysis”, the authors stated that this study adopted the design of a superior test, which is not common in single-arm phase II studies. Please further explain this point.

2.The researchers selected median PFS as the primary endpoint and used historical data as a reference. Please elaborate on the specific parameters and method used in sample size calculation.

3.Some grammatical mistake needs to be corrected.

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## VERSION 1 - AUTHOR RESPONSE

### Reviewer 1 Comments:

1. **Introduction Correction:** Thanks for pointing out. The typo "CAPIAN" has been corrected to "CASPIAN."
2. **Rationale for Therapy Duration:** Thank you for your insightful comment regarding the rationale for the duration of therapy in our study. We have added a discussion on the rationale for the 1-year therapy duration, mainly referred to previous PACIFIC trial and STIMULI trial, and also compared it with the 24-month duration for durvalumab in the ADRIATIC trial.
3. **Inclusion of Recent Studies:** We have included the recent findings from the ASTRUM-005 trial, highlighting its significance for serplulimab as a consolidation therapy option. The statistically significant improvements in OS and PFS from the ADRIATIC trial have been incorporated into the introduction, emphasizing the confirmation of consolidation immunotherapy for LS-SCLC patients who have not progressed after chemoradiotherapy.

### Reviewer 2 Comments:

1. **Explain Serplulimab Combination Treatment:** The introduction has been expanded to better explain the advantages of serplulimab combination treatment. Thanks for your valuable advice.
2. **Discussion Expansion:** The discussion section has been expanded to include a more in-depth analysis of the potential outcomes of serplulimab treatment.

### Reviewer 3 Comments:

1. **Statistical Considerations:** Thanks for the comments. Due to the scale limitations, we designed a single-arm study for comparison with historical data, which is also a viable method in study design. Below are some references. We have also mentioned this in the Strengths and Limitations section.

[1]Park S, Noh JM, Choi YL, et al. Durvalumab with chemoradiotherapy for limited-stage small-cell lung cancer. Eur J Cancer. 2022;169:42-53. doi:10.1016/j.ejca.2022.03.034

[2]Liu C, Zeng L, Deng C, et al. Hypofractionated radiotherapy with immunochemotherapy for extensive-stage small-cell lung cancer. *Front Immunol.* 2023;14:1175960. Published 2023 Jun 7. doi:10.3389/fimmu.2023.1175960

2. **Sample Size Calculation:** In the selection of study endpoints, we mainly referred to the STIMULI study, aiming for an improvement in median PFS with a superiority design. We believe that we have provided a detailed account of the parameters and method used in the sample size calculation in Statistical Considerations and Analysis section. We have also polished this part of the content as suggested. Thanks again for the meticulous examination!
3. **Grammatical Corrections:** The manuscript has been thoroughly reviewed for grammatical errors, and all identified mistakes have been corrected.