Journal of Thoracic Oncology

Case Report: CD103+CD8+ lymphocytes characterize the immune infiltration in a case with pseudoprogression in SqNSCLC.

--Manuscript Draft--

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Manuscript Region of Origin:	SPAIN

To
Keunchil Park, MD, PhD
Associate Editor
Journal of Thoracic Oncology

Dear Professor Park,

We are grateful for the thoughtful comments from the reviewers. We have addressed all points and performed additional required work.

Please find bellow the point by point letter.

We hope you find our revised version acceptable for publication in Journal of Thoracic Oncology.

Yours sincerely,

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Reviewer Comments – Point-by-point response:

Reviewer #1: This is an interesting case report which is hypothesis-generating regarding the explanation of both, lymphocyte infiltration phenotype in ICI-responding tumours as well as pseudoprogression. It expands on previous studies by the group and corroborates its observations by an in vivo observation.

Reply to Reviewer #1:
Thank you for your comment.

Reviewer #2: The authors have submitted a case report of a patient with Stage IV sqNSCLC on PD, treated with Nivolumab with liver pseudo-progression
The liver biopsy unraveled release and expansion of CD103+ TRM as a new potential marker of response even though contributed to the paradox CT increase of the met size.
The case is reported clearly and so are the figures.
The MS is acceptable in the current form.

Reply to Reviewer #2:
Thank you for your comment.

Reviewer #3: Rocha P, et al. reported CD103+CD8+ lymphocytes infiltrated in a pseudoprogression lesion in a squamous NSCLC patient after PD-1 blockade. The finding is somewhat interesting. However, in general CD103 is expressed on activated T cell as well as tissue resident memory (TRM) T cells. So, it was not enough to prove the expansion of "TRM cells' after nivolumab treatments.
TRM cells are found in peripheral tissues that require expression of specific chemo attractants and homing receptors for T-cell recruitment and retention. Authors need to characterize CD103+CD8+T cells more in detail based on its adhesion and migratory properties to distinguish them from activated T cells.

Reply to Reviewer #3:

-Point 1: ‘However, in general CD103 is expressed on activated T cell as well as tissue resident memory (TRM) T cells. So, it was not enough to prove the expansion of TRM cells after nivolumab treatments.’

-Reply to Point 1:

We have answered to this comment below.

As CD103 is a canonical TRM marker on T cells we do not agree with the reviewer that examining TRM-ness or its absence in CD103 positive T cells is a fruitful undertaking. We agree that CD103+ T cells have features of effector (activated) cells and have reported this in our study in Nature Immunology (Ganesan et al, Nature Immunology). Indeed, this observation prompted us to test the expansion of CD103+ cells as presented in this paper. More recent data from patients with lung cancer (Clarke et al, in review) do not identify any CD103+ non-TRM CD8+ cells in lung cancer.

-Point 2: ‘TRM cells are found in peripheral tissues that require expression of specific chemo attractants and homing receptors for T-cell recruitment and retention. Authors need to characterize CD103+CD8+T cells more in detail based on its adhesion and migratory properties to distinguish them from activated T cells.’

-Reply to Point 2:

Thank you for this comment.

In tissue other than cancer tissue, CD103 also defines the TRM population; It is unclear what extra characterization the reviewer wishes to see. CD103 binds to E-cadherin, which is ubiquitously expressed in cancer tissue - further study will not be informative. That TRM exist in other organs is correct but not helpful here as we are not examining possible toxicity. The homing question has already been answered by virtue of the examined T cells tests confirming T cells in the cancer tissue.

Reviewer #4: The authors investigated the immune infiltrate of lesions from pre/post nivolumab therapy samples in an NSCLC patient showing pseudoprogression. Compared to the pre-therapy, lung lesion, the post-therapy, liver lesion showed a marked increase in CD4+ and CD8+ T cells and of CD103+ CD8+ T cells, as documented by both immunohistochemistry and flow cytometry. The implication of this finding is that immunotherapy may contribute to expand this specific T cell subset.

Comments:

It would be relevant to know whether the T cells at tumour site in the on-treatment liver lesion show evidence of proliferation, compared to the pre-therapy lesions. This could be assessed by Ki-67 staining by either immunohistochemistry or flow cytometry. Also, by flow cytometry, it would be relevant to know whether the CD8+ CD103+ T cells in the on-treatment lesion express PD-1. This information, although in a single case, could be relevant to understand whether CD103+ CD8+ T cells may be evaluated as potential biomarkers of responsiveness to anti-PD-1.

Reply to Reviewer #4:

-Point 1: 'It would be relevant to know whether the T cells at tumour site in the on-treatment liver lesion show evidence of proliferation, compared to the pre-therapy lesions. This could be assessed by Ki-67 staining by either immunohistochemistry or flow cytometry.'

-Reply to Point 1:

To address this point, we have performed double immunostaining for Ki67 and CD3 in both samples (lung sample before anti-PD-1 treatment, and liver biopsy after five cycles of Nivolumab). We observed an increase of this marker in lymphocytes in the liver biopsy, which supports our findings.

Illustrative pictures have been added to figure 2 (FIGURE 2A 19 AND 2A 20)

We have also added the results in the manuscript (Highlighted):

Line 44: '*Double staining with Ki67 / CD3 showed a marked increase in the lymphocytes in the liver biopsy compared to pre-treatment lung specimen (Fig 2A19, 2A20).'*

Line 65: *'as demonstrated by increase of Ki67 marker in lymphocytes.'*

Line 128: Figure 2A legend, '*19, 20 CD3 (membrane staining in red) – Ki67 (nucleus staining in brown) double immunostaining, (19) 2 lymphocytes/HPF, (20) 18 lymphocytes/HPF*'.

-Point 2: '*Also, by flow cytometry, it would be relevant to know whether the CD8+ CD103+ T cells in the on-treatment lesion express PD-1. This information, although in a single case, could be relevant to understand whether CD103+ CD8+ T cells may be evaluated as potential biomarkers of responsiveness to anti-PD-1.*'

- Reply Point 2:

We agree with reviewer #4, but unfortunately no remaining fresh tissue is available and the output of lymphocytes in the analysed sample did not allow for the analysis of additional marker. We believe the immunohistochemical data partially overcomes this limitation.

Case Report JTO.

TITLE: Case Report: CD103+CD8+ lymphocytes characterize the immune infiltration in a case with pseudoprogression in SqNSCLC.

SHORT TITLE: CD103+CD8+ T cell expansion in response to nivolumab.

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3. Servei d'Anatomía Patologica. Hospital del Mar, Barcelona, Spain.
4. Servei de Radiología. Hospital del Mar, Barcelona, Spain.
5. Biopharmaceutical New Technologies (BioNTech) Corporation, An der Goldgrube 12, 55131 Mainz, Germany.
6. CR UK and NIHR Experimental Cancer Medicine Centre Southampton, University of Southampton, Faculty of Medicine, Tremona Road, Southampton SO166YD, UK.

*These authors equally contributed to the work

CASE:

A 65-year-old male patient, current smoker was diagnosed with stage IV squamous cell lung cancer (multiple CNS lesions) (Fig 1A, B). He received whole-brain radiotherapy followed by chemotherapy with Carboplatin (AUC 5) – Vinorelbine (25mg/m2). After three cycles, disease progression was confirmed, with an increase of the lung tumor and development of new liver lesions (Fig 1C, D). Nivolumab was then initiated. At radiologic evaluation, after five cycles of Nivolumab, a discordant response was observed, with partial response in the CNS, stable lung disease but significant increase of one liver lesion (Fig 1E, F). The marked discrepancy between the clinical benefit and the radiological findings, prompted us to perform a liver biopsy.

The pathological findings revealed extensive areas of necrosis, no viable tumor cells and the presence of a lymphohistiocytic infiltrate.

Immune biomarkers were compared between the lung biopsy at diagnosis and the liver biopsy after five cycles of Nivolumab by immunohistochemistry (IHC) (Fig 2A1, 2A2). All tumor cells (100%) expressed PD-L1 pretreatment and were necrotic in the on-treatment biopsy (Fig 2A3, Fig 2A4). Lymphocyte characterization revealed increased numbers of CD4 (Fig 2A7, 2A8), and CD8 (Fig 2A9, 2A10) in the on-treatment biopsy, with a change in the ratio of CD4/CD8 (at diagnosis 1.25, and 0.875 after treatment with ICI). CD103 (Fig 2A11, 2A12) positive cells were also increased in the liver biopsy, and CD68 staining demonstrated a higher proportion of macrophages in the liver biopsy (Fig 2A13, 2A14). PD-1 expression was observed in macrophages and lymphocytes and was also enhanced in the on-treatment liver biopsy (Fig 2A17, 2A18). Double staining with Ki67 / CD3 showed a marked increase in the lymphocytes in the liver biopsy compared to pre-treatment lung specimen (Fig 2A19, 2A20).

In order to further characterize the lymphocyte populations observed in the on-treatment liver biopsy by IHC, we performed FACS analysis. Of the live lymphocytes (Fig 2BI), 55% were TCR+ (Fig 2BII) and within this gate 65.2% expressed CD8a, 29.8% CD4 (Fig 2BIII). Consistent with the IHC staining, the majority of CD8 T cells (69.6%) co-expressed the tissue residency marker CD103 (Fig. 2BIV).

DISCUSSION:

New patterns of radiologic response have been described with immune checkpoints inhibitors (ICI), such as pseudoprogression and mixed responses (1,2). Biopsies of the ‘growing’ lesion have demonstrated lymphocyte infiltration as a cause of this initial increase in size (3,4).

We have recently reported that CD103+ Tissue resident memory (TRM) CD8+ T cells are protective in early lung cancer (5). The pretreatment biopsy of our patient showed the presence of CD8+CD103+ T cells. Characterization of immune population by IHC and FACS in the on-treatment sample demonstrated a substantial increase in CD8+CD103+ T cells in the liver metastasis, compared to pretreatment density.

Our data show for the first time that PD-1 blockade might therefore not only enhance the activation and proliferation of immune competent T cells globally, but may also contribute to effective responses through release and expansion of CD103+ TRM cells as demonstrated by increase of Ki67 marker in lymphocytes. The influx or intratumoral expansion of protective immune cells presented clinically as tumor volume increase. Our data offer a morphological insight to understand clinical correlates of an antitumor response that can be released in lung cancer through checkpoint blockade.

REFERENCES:

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FIGURE LEGENDS:

Figure 1. CT scan at diagnosis (August 2016) (A and B), pre Nivolumab treatment (C and D) and after five cycles of Nivolumab (E and F). A and B images show a lung mass of 45 mm (A, arrow), localized in the upper left upper lobe. This lesion presents extensive contact with the pulmonary artery and compromises the distal airway. In the abdominal CT scan from the same date (B) no liver lesions were observed. The radiologic evaluation made in December 2016, revealed an increase in the size of the lung lesion (C) (45mm to 48mm) and greater obstruction of the distal airway. In the same study, abdominal CT scan revealed the appearance of a hepatic lesion (D) (yellow circle) of 20mm, accounting for progressive disease.

Subsequent CT scan after five cycles of Nivolumab, showed a decrease in the size of lung mass (E) of 48 mm to 45mm, and increase in size of the hepatic metastatic lesion (F) (yellow circle) from 20 to 33mm. RECIST 1.1 + 14.7%. (two target lesions). But an increase of 65% at the liver lesion.

Figure 2A. Histological assessment of lung and liver biopsy. 1, 3, 5, 7, 9, 11, 13, 15, 17 (left column) corresponding to lung biopsy at diagnosis. 2, 4, 6, 8, 10, 12, 14, 16, 18 (right column) corresponding to liver biopsy after five cycles of nivolumab.

1 and 2 H&E staining, 1 - revealed a poorly differentiated squamous carcinoma, and 2.a dense lymphohistiocytic infiltrate surrounding a totally necrotic metastatic tumour. 3 and 4 PD-L1 staining, 100% in tumour cells of lung biopsy and high expression in macrophages and lymphocytes. 5,6 CD3 staining, (5) 75 lymphocytes/HPF, and (6) 250 lymphocytes/HPF. 7, 8 staining for CD4 marker, (7) 50 lymphocytes/HPF, (8) 140 lymphocytes/HPF. 9, 10 CD8 staining (9) 40 lymphocytes/HPF, (10) 160 lymphocytes/HPF. 11, 12 CD103 staining, (11) 15 lymphocytes/HPF, (12) 100

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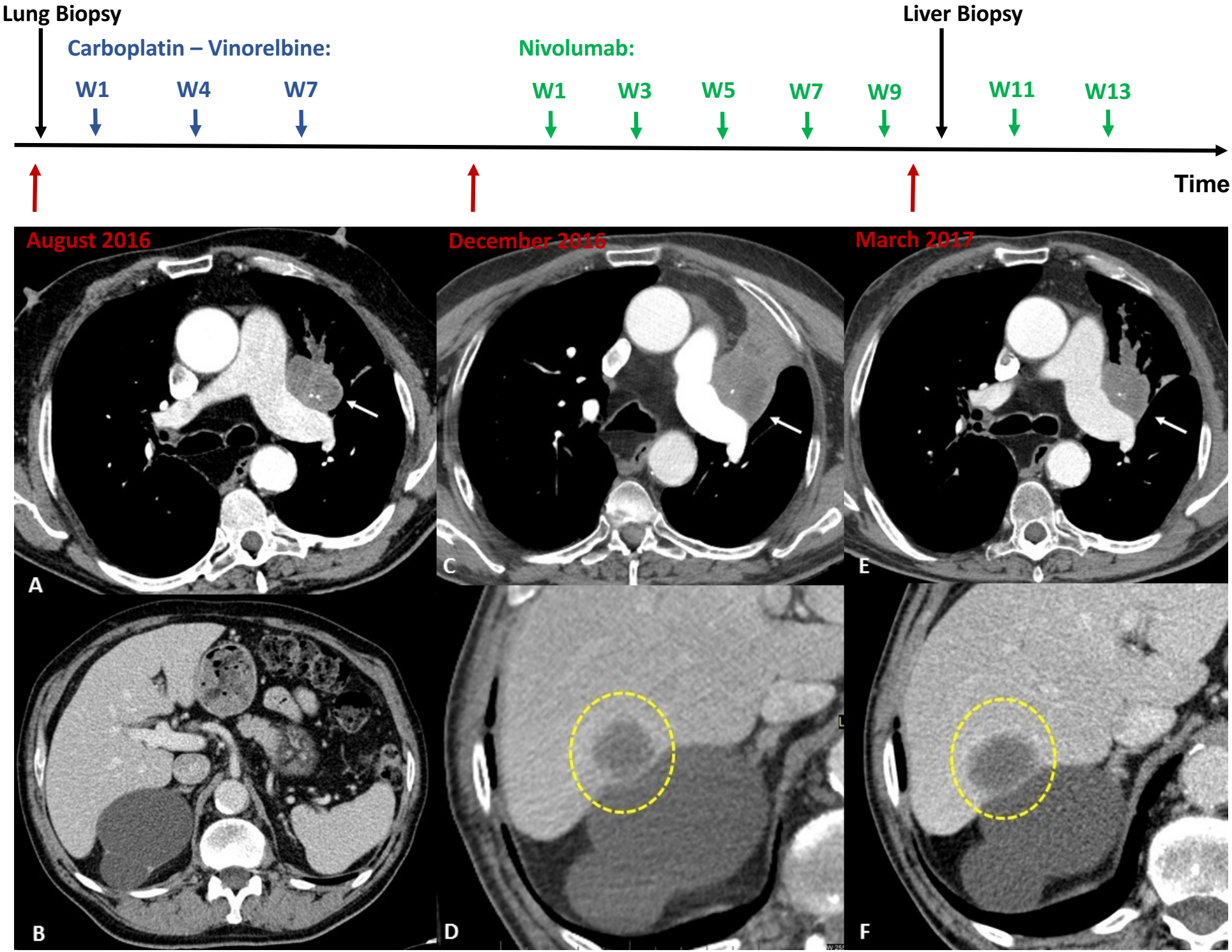
Figure 1


Lung Biopsy
Carboplatin – Vinorelbine:
W1
W4
W7
Nivolumab:
W1
W3
W5
W7
W9
Liver Biopsy
W11
W13
Time
August 2016
December 2016
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A
B
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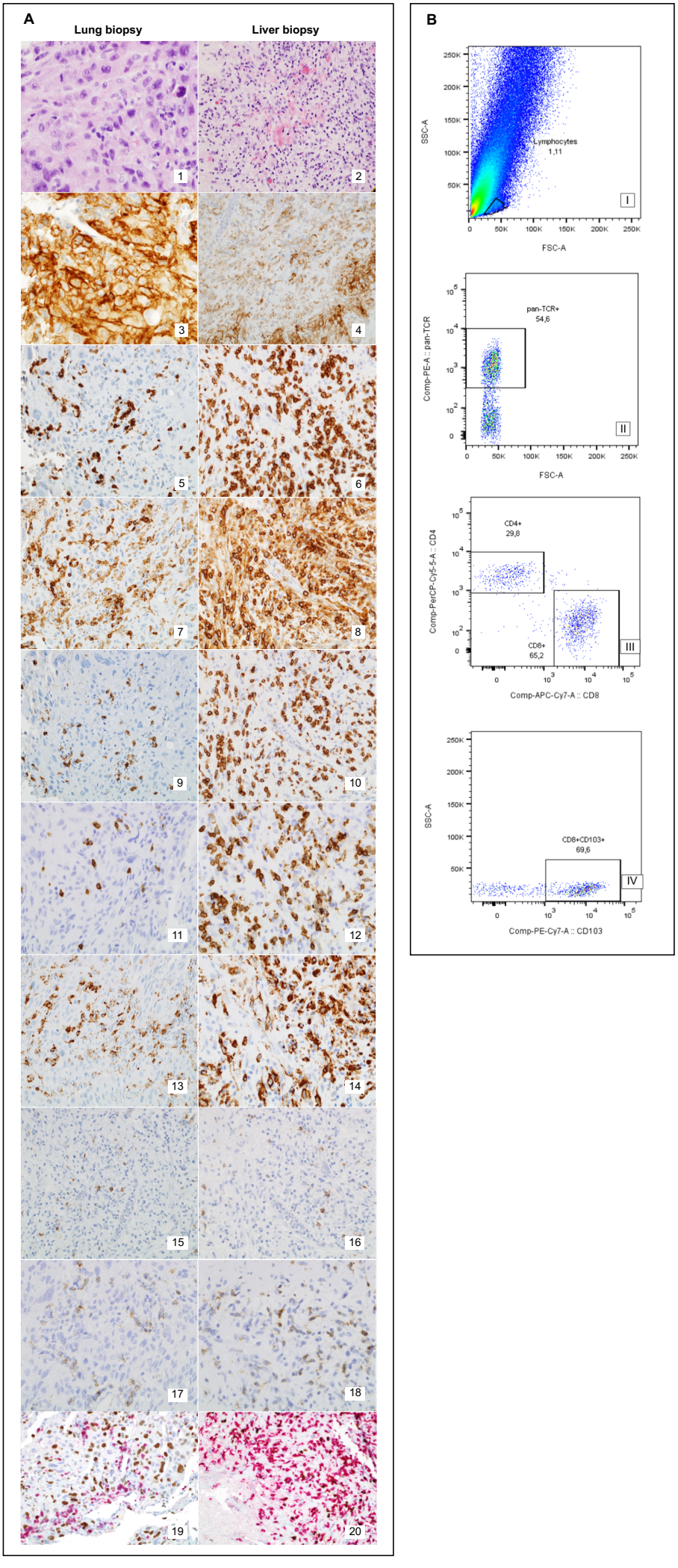
Figure 2


A
Lung biopsy
Liver biopsy
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13
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17
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B
SSC-A
FSC-A
Lymphocytes
1,11
I
Comp-PE-A :: pan-TCR
pan-TCR+
54,6
II
Comp-PerCP-Cy5-5-A :: CD4
Comp-APC-Cy7-A :: CD8
CD4+
29,8
CD8+
65,2
III
CD8+CD103+
69,6
IV
Comp-PE-Cy7-A :: CD103

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Instructions

The purpose of this form is to provide readers of your manuscript with information about your other interests that could influence how they receive and understand your work. The form is designed to be completed electronically and stored electronically. It contains programming that allows appropriate data display. Each author should submit a separate form and is responsible for the accuracy and completeness of the submitted information. The form is in six parts.

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2. The work under consideration for publication.

This section asks for information about the work that you have submitted for publication. The time frame for this reporting is that of the work itself, from the initial conception and planning to the present. The requested information is about resources that you received, either directly or indirectly (via your institution), to enable you to complete the work. Checking "No" means that you did the work without receiving any financial support from any third party -- that is, the work was supported by funds from the same institution that pays your salary and that institution did not receive third-party funds with which to pay you. If you or your institution received funds from a third party to support the work, such as a government granting agency, charitable foundation or commercial sponsor, check "Yes".

3. Relevant financial activities outside the submitted work.

This section asks about your financial relationships with entities in the bio-medical arena that could be perceived to influence, or that give the appearance of potentially influencing, what you wrote in the submitted work. You should disclose interactions with ANY entity that could be considered broadly relevant to the work. For example, if your article is about testing an epidermal growth factor receptor (EGFR) antagonist in lung cancer, you should report all associations with entities pursuing diagnostic or therapeutic strategies in cancer in general, not just in the area of EGFR or lung cancer.

Report all sources of revenue paid (or promised to be paid) directly to you or your institution on your behalf over the 36 months prior to submission of the work. This should include all monies from sources with relevance to the submitted work, not just monies from the entity that sponsored the research. Please note that your interactions with the work's sponsor that are outside the submitted work should also be listed here. If there is any question, it is usually better to disclose a relationship than not to do so.

For grants you have received for work outside the submitted work, you should disclose support ONLY from entities that could be perceived to be affected financially by the published work, such as drug companies, or foundations supported by entities that could be perceived to have a financial stake in the outcome. Public funding sources, such as government agencies, charitable foundations or academic institutions, need not be disclosed. For example, if a government agency sponsored a study in which you have been involved and drugs were provided by a pharmaceutical company, you need only list the pharmaceutical company.

4. Intellectual Property.

This section asks about patents and copyrights, whether pending, issued, licensed and/or receiving royalties.

5. Relationships not covered above.

Use this section to report other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, what you wrote in the submitted work.

Definitions.

Entity: government agency, foundation, commercial sponsor, academic institution, etc.
Grant: A grant from an entity, generally [but not always] paid to your organization
Personal Fees: Monies paid to you for services rendered, generally honoraria, royalties, or fees for consulting , lectures, speakers bureaus, expert testimony, employment, or other affiliations
Non-Financial Support: Examples include drugs/equipment supplied by the entity, travel paid by the entity, writing assistance, administrative support, etc.
Other: Anything not covered under the previous three boxes
Pending: The patent has been filed but not issued
Issued: The patent has been issued by the agency
Licensed: The patent has been licensed to an entity, whether earning royalties or not
Royalties: Funds are coming in to you or your institution due to your patent

ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name): Pedro
2. Surname (Last Name): Rocha
3. Date: 06-March-2018

4. Are you the corresponding author? ☐ Yes ☑ No

Corresponding Author's Name: Edurne Arriola

5. Manuscript Title: Case Report: CD103+CD8+ lymphocytes characterize the immune infiltration in a case with pseudoprogression in SqNSCLC

6. Manuscript Identifying Number (if you know it):

Section 2. The Work Under Consideration for Publication

Did you or your institution **at any time** receive payment or services from a third party (government, commercial, private foundation, etc.) for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc.)?

Are there any relevant conflicts of interest? ☐ Yes ☑ No

Section 3. Relevant financial activities outside the submitted work.

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Are there any relevant conflicts of interest? ☐ Yes ☑ No

Section 4. Intellectual Property -- Patents & Copyrights

Do you have any patents, whether planned, pending or issued, broadly relevant to the work? ☐ Yes ☑ No

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Section 5. Relationships not covered above

Are there other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, what you wrote in the submitted work?

☐ Yes, the following relationships/conditions/circumstances are present (explain below):

☑ No other relationships/conditions/circumstances that present a potential conflict of interest

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Section 6. Disclosure Statement

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Dr. Rocha has nothing to disclose.

Evaluation and Feedback

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Non-Financial Support: Examples include drugs/equipment supplied by the entity, travel paid by the entity, writing assistance, administrative support, etc.
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ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name): Álvaro
2. Surname (Last Name): Taus
3. Date: 06-March-2018

4. Are you the corresponding author? ☐ Yes ☑ No

Corresponding Author's Name: Edurne Arriola

5. Manuscript Title: Case Report: CD103+CD8+ lymphocytes characterize the immune infiltration in a case with pseudoprogression in SqNSCLC.

6. Manuscript Identifying Number (if you know it):

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Are there any relevant conflicts of interest? ☐ Yes ☑ No

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Are there any relevant conflicts of interest? ☑ Yes ☐ No

If yes, please fill out the appropriate information below.

Name of Entity	Grant?	Personal Fees?	Non-Financial Support?	Other?	Comments
Merck Sharp & Dohme	☐	☑	☐	☐	
Bristol-Myers Squibb	☐	☑	☐	☐	

Section 4. Intellectual Property -- Patents & Copyrights

Do you have any patents, whether planned, pending or issued, broadly relevant to the work? ☐ Yes ☑ No

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Section 5. Relationships not covered above

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Section 6. Disclosure Statement

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Dr. Taus reports personal fees from Merck Sharp & Dohme, personal fees from Bristol-Myers Squibb, outside the submitted work; .

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4. Intellectual Property.

This section asks about patents and copyrights, whether pending, issued, licensed and/or receiving royalties.

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Non-Financial Support: Examples include drugs/equipment supplied by the entity, travel paid by the entity, writing assistance, administrative support, etc.
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Licensed: The patent has been licensed to an entity, whether earning royalties or not
Royalties: Funds are coming in to you or your institution due to your patent

ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name): Christian
2. Surname (Last Name): Ottensmeier
3. Date: 06-March-2018

4. Are you the corresponding author? ☐ Yes ☑ No Corresponding Author's Name:

5. Manuscript Title: Case Report: CD103+CD8+ lymphocytes characterize the immune infiltration in a case with pseudoprogression in SqNSCLC

6. Manuscript Identifying Number (if you know it):

Section 2. The Work Under Consideration for Publication

Did you or your institution **at any time** receive payment or services from a third party (government, commercial, private foundation, etc.) for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc.)?

Are there any relevant conflicts of interest? ☐ Yes ☐ No

Section 3. Relevant financial activities outside the submitted work.

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Are there any relevant conflicts of interest? ☑ Yes ☐ No

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Name of Entity	Grant?	Personal Fees?	Non-Financial Support?	Other?	Comments
Bristol-Myers Squibb	☑	☑	☐	☐	
Merck Sharp & Dohme	☑	☑	☐	☐	
Immatics	☐	☑	☐	☐	
Verastem	☑	☐	☐	☐	
BioNTech AG	☑	☐	☐	☐	
Delcath Systems	☑	☐	☐	☐	
Serametrix	☑	☐	☐	☐	
Inovio Pharmaceuticals	☑	☐	☐	☐	

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Section 4. Intellectual Property -- Patents & Copyrights

Do you have any patents, whether planned, pending or issued, broadly relevant to the work? ☐ Yes ☑ No

Section 5. Relationships not covered above

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Dr. Ottensmeier reports grants and personal fees from Bristol-Myers Squibb, grants and personal fees from Merck Sharp & Dohme, personal fees from Immatics, grants from Verastem, grants from BioNTech AG, grants from Delcath Systems, grants from Serametrix, grants from Inovio Pharmaceuticals, outside the submitted work; .

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ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name): Dolores
2. Surname (Last Name): Naranjo
3. Date: 06-March-2018

4. Are you the corresponding author? ☐ Yes ☑ No

Corresponding Author's Name

5. Manuscript Title

Case Report: CD103+CD8+ lymphocytes characterize the immune infiltration in a case with pseudoprogression in SqNSCLC.

6. Manuscript Identifying Number (if you know it)

Section 2. The Work Under Consideration for Publication

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Are there any relevant conflicts of interest? ☐ Yes ☑ No

Section 4. Intellectual Property -- Patents & Copyrights

Do you have any patents, whether planned, pending or issued, broadly relevant to the work? ☐ Yes ☑ No

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Dr. Naranjo has nothing to disclose.

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Royalties: Funds are coming in to you or your institution due to your patent

ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name): Edurne
2. Surname (Last Name): Arriola
3. Date: 06-March-2018

4. Are you the corresponding author? ☑ Yes ☐ No

5. Manuscript Title
Case Report: CD103+CD8+ lymphocytes characterize the immune infiltration in a case with pseudoprogression in SqNSCLC

6. Manuscript Identifying Number (if you know it)

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Are there any relevant conflicts of interest? ☐ Yes ☐ No

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Are there any relevant conflicts of interest? ☑ Yes ☐ No

If yes, please fill out the appropriate information below.

Name of Entity	Grant?	Personal Fees?	Non-Financial Support?	Other?	Comments
Merck Sharp & Dohme	☐	☑	☐	☐	
Bristol-Myers Squibb	☐	☑	☐	☐	
Roche	☑	☑	☐	☐	

Section 4. Intellectual Property -- Patents & Copyrights

Do you have any patents, whether planned, pending or issued, broadly relevant to the work? ☐ Yes ☑ No

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Royalties: Funds are coming in to you or your institution due to your patent

ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name): Flavio
2. Surname (Last Name): Zuccarino
3. Date: 06-March-2018

4. Are you the corresponding author? ☐ Yes ☑ No

Corresponding Author's Name: Edurne Arriola

5. Manuscript Title

Case Report: CD103+CD8+ lymphocytes characterize the immune infiltration in a case with pseudoprogression in SqNSCLC.

6. Manuscript Identifying Number (if you know it)

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Are there any relevant conflicts of interest? ☐ Yes ☑ No

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Are there any relevant conflicts of interest? ☐ Yes ☑ No

Section 4. Intellectual Property -- Patents & Copyrights

Do you have any patents, whether planned, pending or issued, broadly relevant to the work? ☐ Yes ☑ No

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Dr. Zuccarino has nothing to disclose.

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Section 1. Identifying Information

1. Given Name (First Name): Maite
2. Surname (Last Name): Rodrigo
3. Date: 06-March-2018

4. Are you the corresponding author? ☐ Yes ☑ No

Corresponding Author's Name: Edurne Arriola

5. Manuscript Title

Case Report: CD103+CD8+ lymphocytes characterize the immune infiltration in a case with pseudoprogression in SqNSCLC.

6. Manuscript Identifying Number (if you know it)

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Section 1. Identifying Information

1. Given Name (First Name): Max
2. Surname (Last Name): Hardy-Werbin
3. Date: 06-March-2018

4. Are you the corresponding author? ☐ Yes ☑ No

Corresponding Author's Name:

5. Manuscript Title: Case Report: CD103+CD8+ lymphocytes characterize the immune infiltration in a case with pseudoprogression in SqNSCLC.

6. Manuscript Identifying Number (if you know it):

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Section 1. Identifying Information

1. Given Name (First Name): Oliver
2. Surname (Last Name): Wood
3. Date: 06-March-2018

4. Are you the corresponding author? ☐ Yes ☑ No

Corresponding Author's Name: Edurne Arriola

5. Manuscript Title: Case Report: CD103+CD8+ lymphocytes characterize the immune infiltration in a case with pseudoprogression in SqNSCLC.

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Dr. Wood has nothing to disclose.

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Section 1. Identifying Information

1. Given Name (First Name): René
2. Surname (Last Name): Roth
3. Date: 06-March-2018

4. Are you the corresponding author? ☐ Yes ☑ No

Corresponding Author's Name: Edurne Arriola

5. Manuscript Title: Case Report: CD103+CD8+ lymphocytes characterize the immune infiltration in a case with pseudoprogression in SqNSCLC.

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