

# RECIST 1.1 evaluations in a phase II clinical trial:

Does reader expertise represent a risk factor for measure reliability?

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the **bigger picture**

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# Conflict of interest

**Employee at MEDIAN Technologies**

# Background

Double read settings  
in clinical trials



## Goals:

- Reduces errors
- Increases quality
- Ensure consistency
- Avoid bias

## Risk:

- Inter-reader discordances

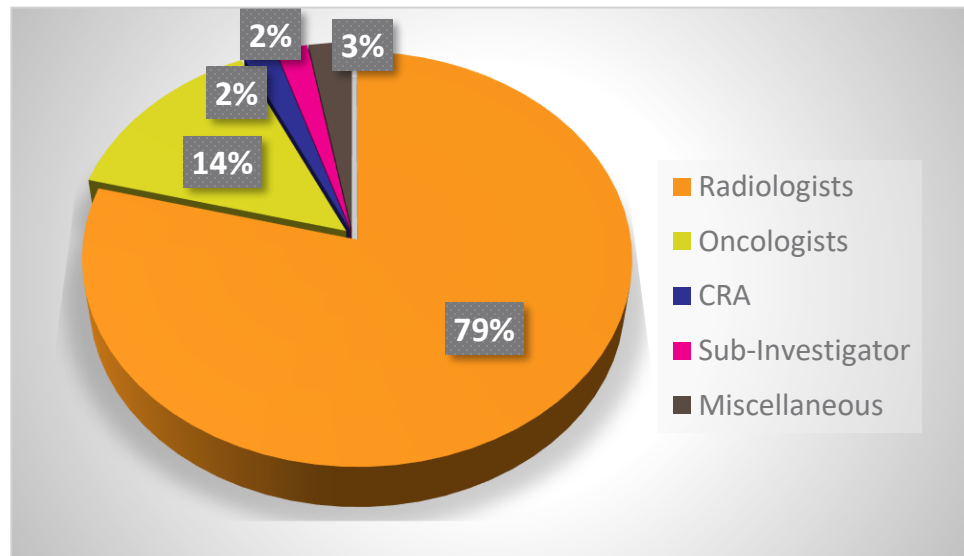
**Purpose of the study: To analyze risk factors likely to produce inter-reader discordances in a RECIST 1.1 trial**

# Materials

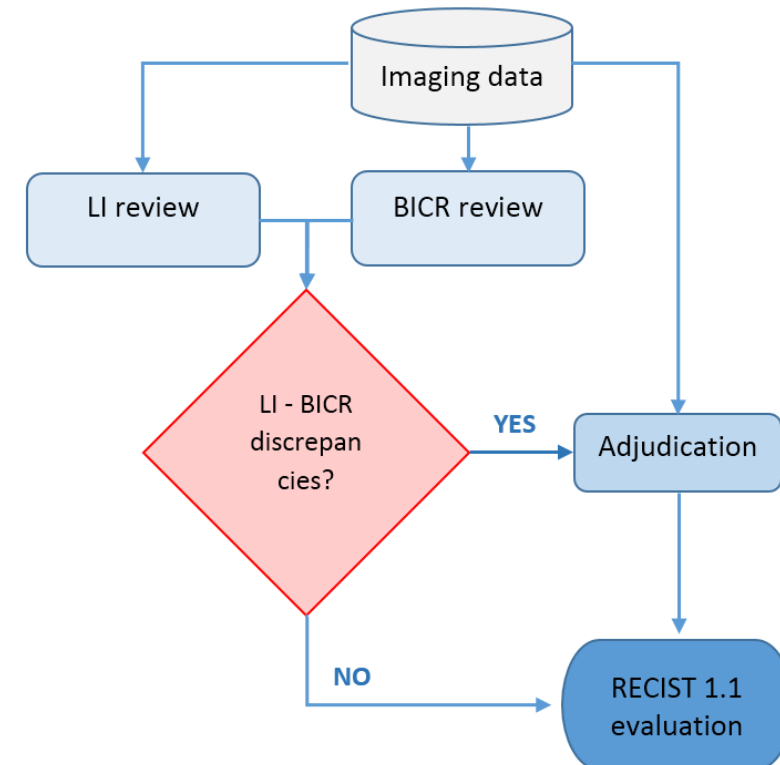
## Analysis of a real clinical trial: ARD12166

### About the clinical trial:

- Phase II study
- Indication: Small Cell Lung Cancer
- Imaging criteria: RECIST 1.1
- Cohort: 147 patients
- Different readers' qualifications:



### Imaging workflow: Double read: Local/central read + adjudication



# Methods

## Step 1

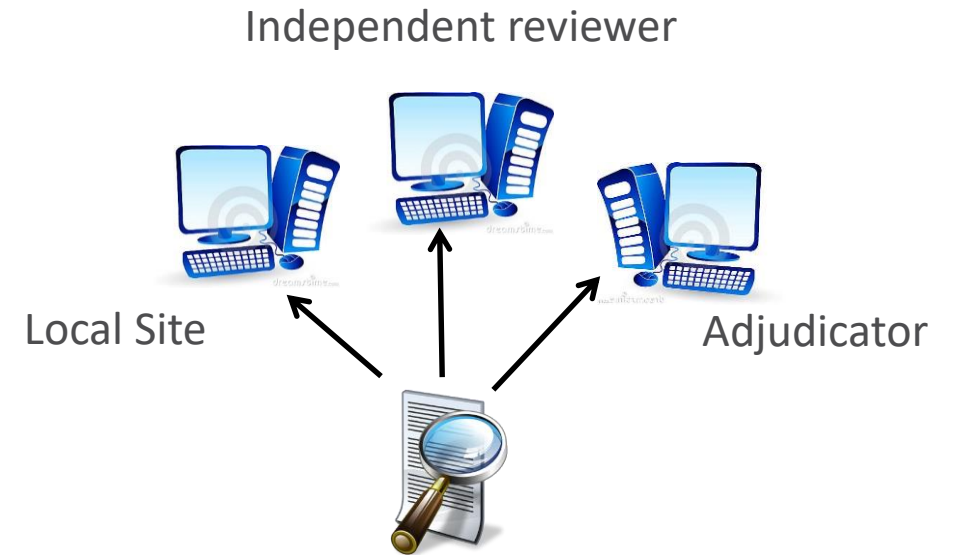
Two experts (10Y+) compared all:

1. Radiology reports
2. Annotations
3. Images

from all readers (local site reader, independent reviewer and adjudicator)

## Step 2

We correlated the comparisons to the discordances in declaring progressive disease according to RECIST 1.1



Risk factors were: **differences in reports, annotations, images and readers expertise** leading to **inter-reader discordances**

# Tested Risks factors

## *Tumors, Images and... Readers*

The predefinition of risk factors was based on a literature review and RECIST guidelines

### As a reminder: RECIST 1.1 summary

1. 5 max. target lesions
2. Detection of new lesions
3. Subjective assessment of non target

### New response evaluation criteria in solid tumours: Revised RECIST guideline (version 1.1)

E.A. Eisenhauer<sup>a,\*</sup>, P. Therasse<sup>b</sup>, J. Bogaerts<sup>c</sup>, L.H. Schwartz<sup>d</sup>, D. Sargent<sup>e</sup>, R. Ford<sup>f</sup>, J. Dancey<sup>g</sup>, S. Arbuuck<sup>h</sup>, S. Gwyther<sup>i</sup>, M. Mooney<sup>g</sup>, L. Rubinstein<sup>g</sup>, L. Shankar<sup>g</sup>, L. Dodd<sup>g</sup>, R. Kaplan<sup>j</sup>, D. Lacombe<sup>c</sup>, J. Verweij<sup>k</sup>

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### Risk factors

1. Different scans at baseline
2. Different scan(s) at follow up
3. Different number of target lesions
4. New lesions
5. Different target lesions
6. Non measurable lesions
7. Progressive non-target lesions

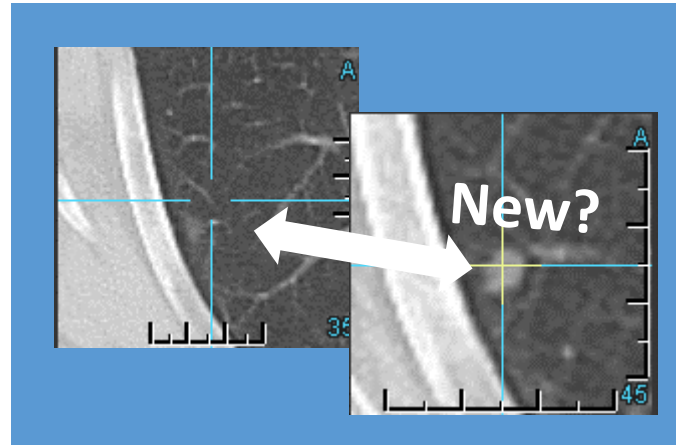
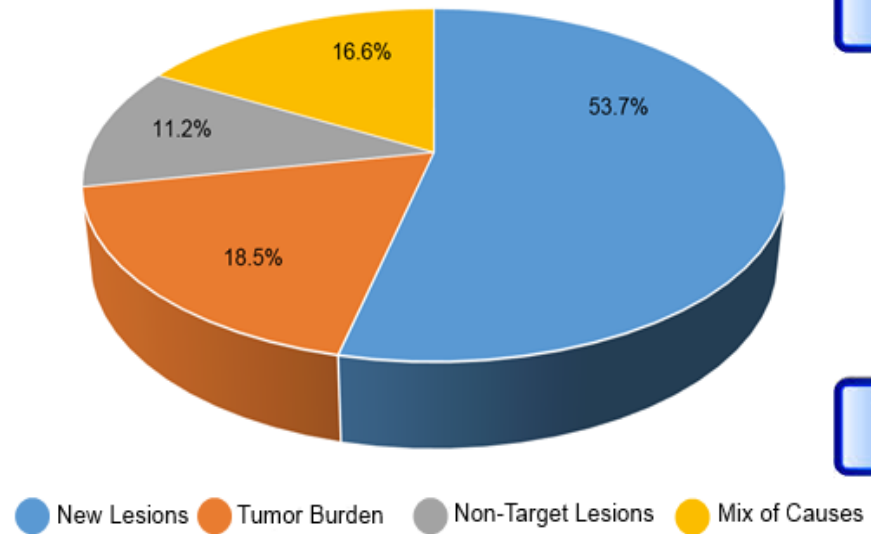
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### Reader's expertise

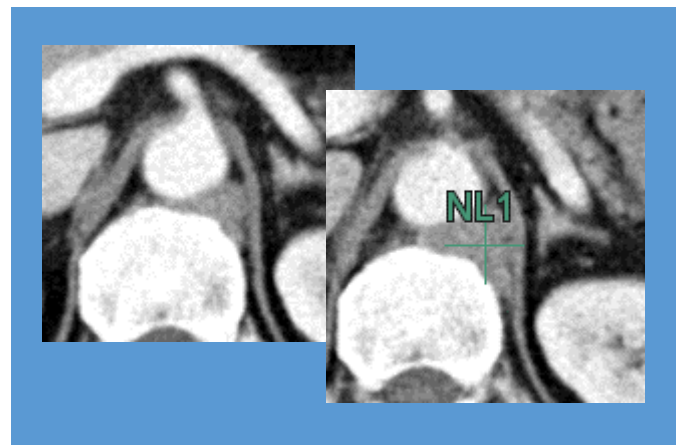


# Results

## *Distribution of discrepancies - Relevant Risk factors*



Largest cause of discrepancy and major risk factor: new lesion



The majority of questionable new lesions: new nodal lesions

# Results

## Irrelevant risk factors

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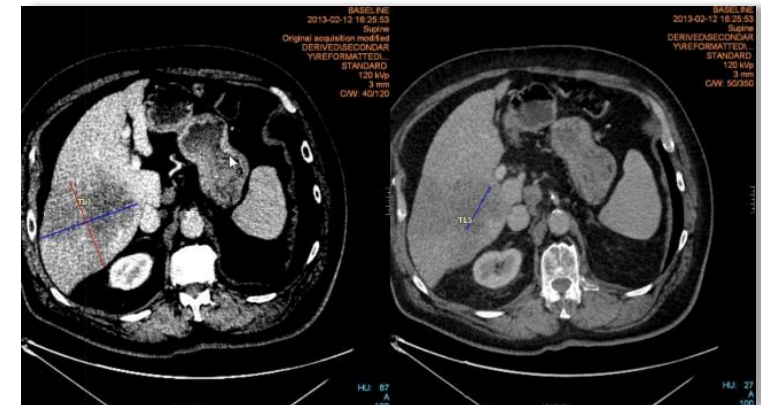
Regarding reader's expertise, the adjudication rate was not different between radiologists and non-radiologists:

- Globally ( $p=0.28$ )
- Related to the detection of new lesions ( $p=0.52$ )

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Other not proven risk for (pValue):

Selection of non-measurable lesions	( $p=0.25$ )
Different series selected at baseline	( $p=1.0$ )
Different series selected for follow up	( $p=0.2$ )
Different selection of target lesions	( $p=0.06$ )





# Conclusions

- Readers expertise was not proven to be a significant risk factor
- New lesions detection was confirmed as a major issue
- The detection of increased tumor burden was the second risk factor of discrepancy
- Quality readers selection, training and monitoring allowed involving different readers expertise



# Thank you!

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