

A Torrente-López<sup>1</sup>, J Herмосilla Fernández<sup>1</sup>, J Hernández Jiménez<sup>1</sup>, J Cabeza<sup>2</sup>, A Salmerón García<sup>2</sup>, N Navas<sup>1</sup>

<sup>1</sup>Biomedical Research Institute Ibs Granada, Analytical Chemistry-Science Faculty-University of Granada, Granada, Spain

<sup>2</sup>Biomedical Research Institute Ibs Granada, Clinical Pharmacy-San Cecilio University Hospital, Granada, Spain

anabelt@ugr.es

3PC-065  
ATC code: L03

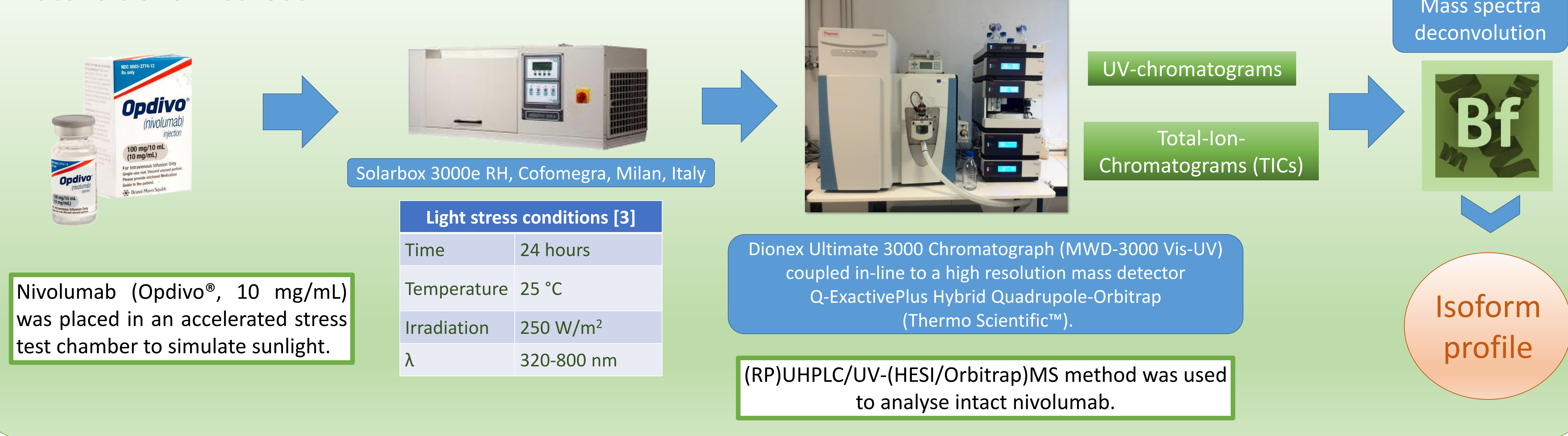
## Background and importance

Nivolumab (Opdivo®) is a human IgG4 monoclonal antibody (mAb) from the group of immunomodulators, which binds to programmed death receptor 1 (PD-1). As a complex protein, physical aggregation and chemical degradation can occur throughout its life, and even modest environmental stresses could cause extensive damage [1]. As indicated in its technical report [2], the unopened vials can be stored at controlled room temperature up to 25 °C with room light for up to 48 hours.

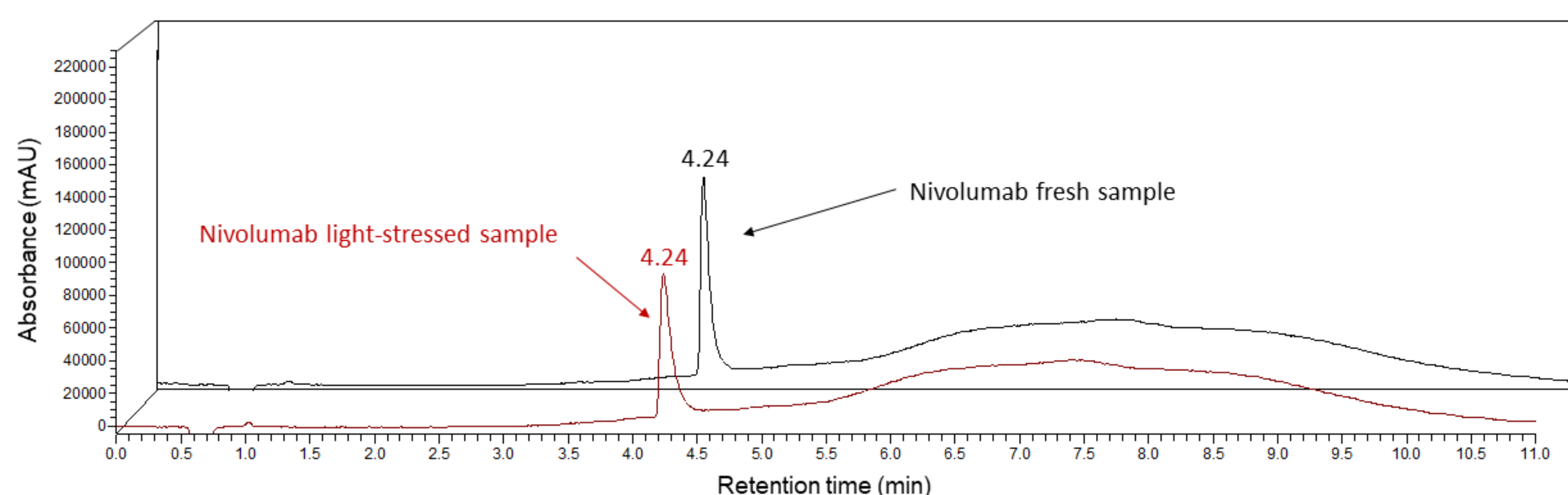
## Aim and objectives

To assess the impact on the isoforms profile of nivolumab 10 mg/mL (Opdivo®) promoted by exposure to light in its own opened vial at controlled temperature of 25 °C to evaluate likely risks from unintentional mishandling in real hospital conditions.

## Materials and methods

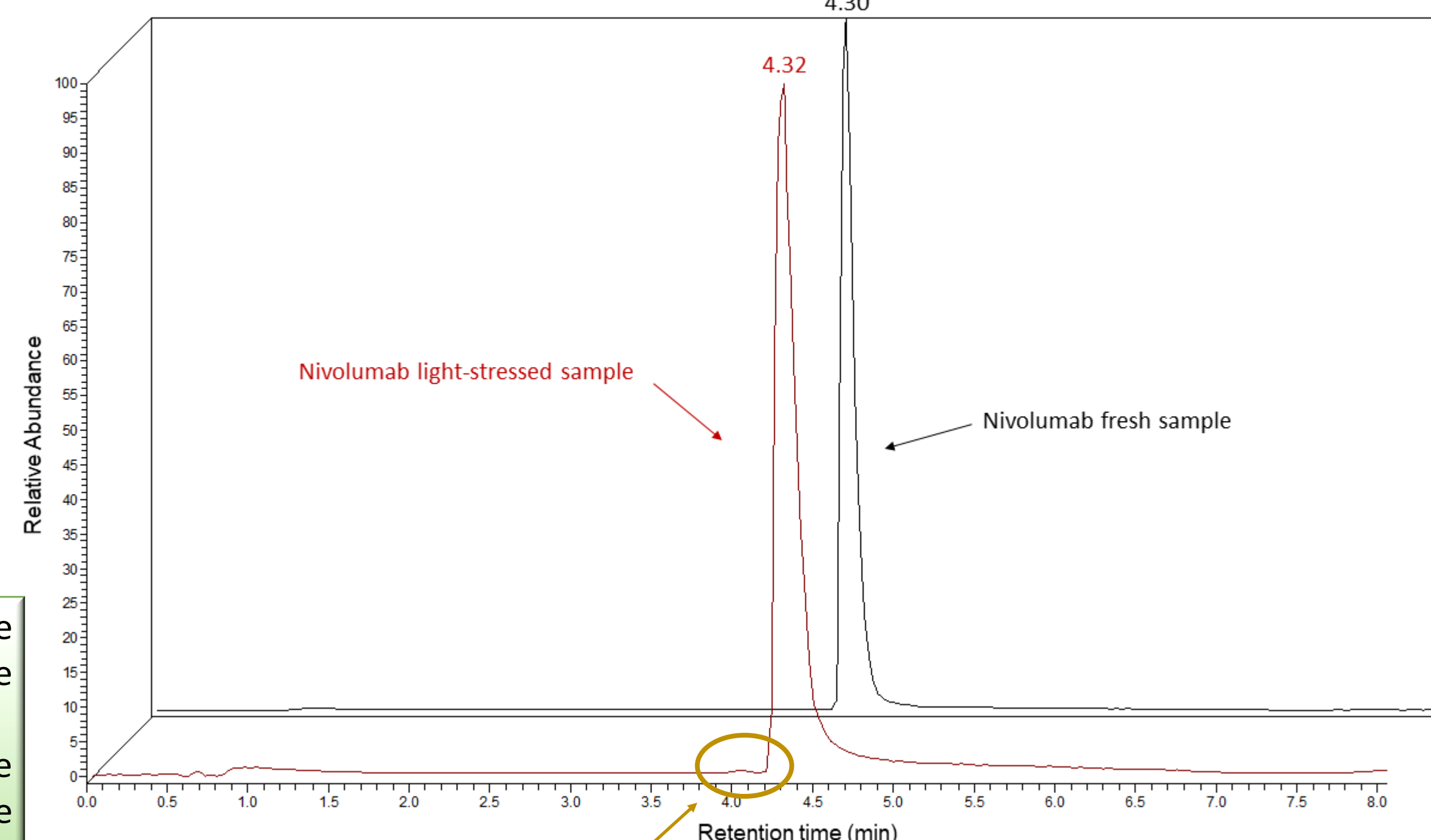


## UV-Chromatograms (nivolumab 25 ppm)



## Results

## Total Ions Chromatograms -TICs- (nivolumab 25 ppm)

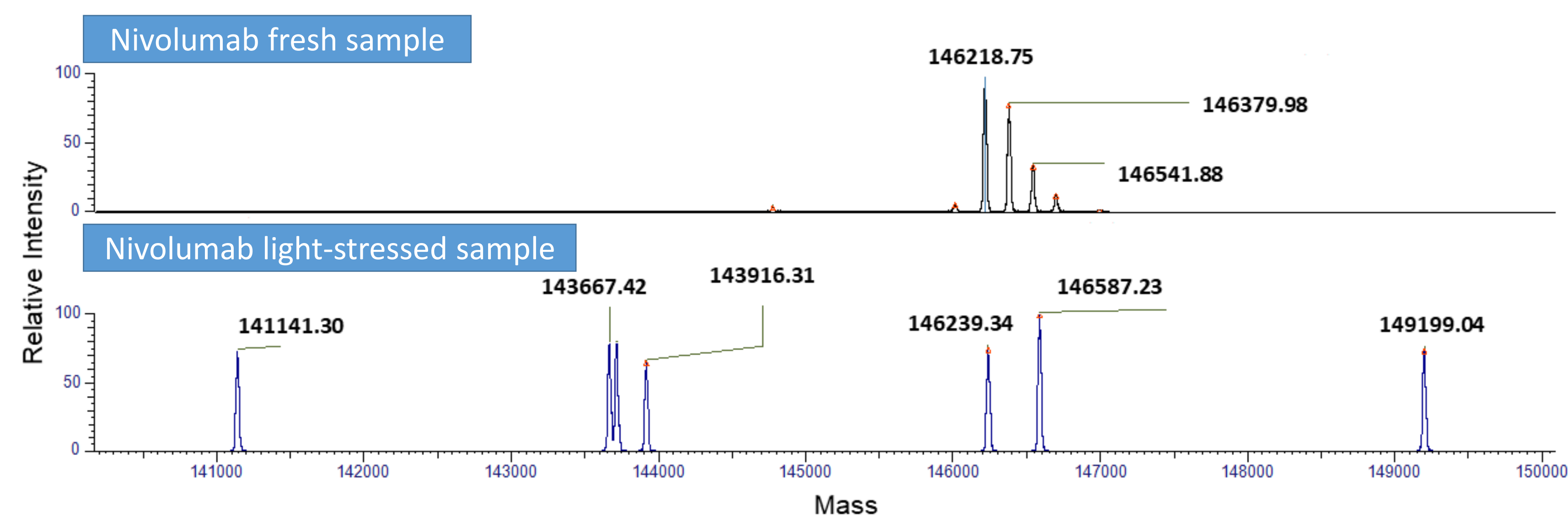


## Areas under the chromatographic peaks

	Main nivolumab peak	New detected peak
<b>UV-chromatograms</b>		
Fresh sample	598728	-
Light-stressed sample	547360	-
<b>TICs</b>		
Fresh sample	2261962118	294532
Light-stressed sample	1027546630	2617368

- A decrease in the area of the chromatographic peaks corresponding to the light-stressed sample was observed.  
- A new peak was detected right before the main nivolumab chromatographic peak in the TIC corresponding to the light-stressed sample.

## Mass spectrometric isoforms profile (nivolumab 25 ppm)



**Isoforms profile clearly evidenced changes in the light-submitted nivolumab samples.** An important increase in the number of isoforms even with changes in their masses -including the main isoform- was detected.

## Conclusion and relevance

The exposure to light may cause modifications in the nivolumab isoform profile which suggests protein degradation. This has been confirmed by the results obtained. The current work shows the importance of protecting from light the opened vials of the medicine Opdivo® (and for extension, the bags for infusion), when they are placed at room temperature (up to 25 °C).

[1] M.R.Nejadnik et al. J.Pharm.Sc.107(2018)2013-2019.

[2] Nivolumab Technical Report: [https://www.ema.europa.eu/en/documents/product-information/opdivo-epar-product-information\\_en.pdf](https://www.ema.europa.eu/en/documents/product-information/opdivo-epar-product-information_en.pdf)

[3] Scientific discussion ICH Q1B photostability testing of new active substances and medicinal products. European Medicines Agency (EMA); 1998: [https://www.ema.europa.eu/en/documents/scientific-guideline/ich-q1-b-photostability-testing-new-active-substances-medicinal-products-step-5\\_en.pdf](https://www.ema.europa.eu/en/documents/scientific-guideline/ich-q1-b-photostability-testing-new-active-substances-medicinal-products-step-5_en.pdf)