

# IN USE PHYSICOCHEMICAL AND MICROBIOLOGICAL STABILITY OF DILUTED SOLUTIONS OF THE MONOCLONAL ANTIBODY NIVOLUMAB

M. RIVANO<sup>1</sup>, F. SELMIN<sup>2</sup>, L. CAMUFFO<sup>1</sup>, L. CANCELLI<sup>1</sup>, G. MANGONI<sup>1</sup>, M.A. PICCOLI<sup>1</sup>, G. LONGOBARDO<sup>3</sup>, F. CILURZO<sup>2</sup>, P. MINGHETTI<sup>2</sup>

<sup>1</sup>UNIVERSITY OF MILAN, SCHOOL OF HOSPITAL PHARMACY, MILAN, ITALY

<sup>2</sup>UNIVERSITY OF MILAN, DEPARTMENT OF PHARMACEUTICAL SCIENCES, MILAN, ITALY

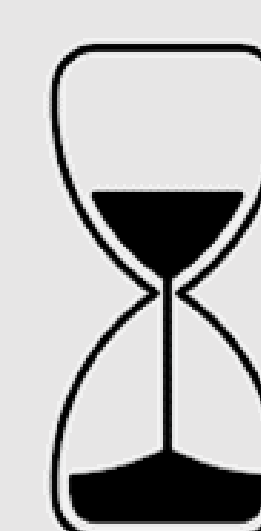
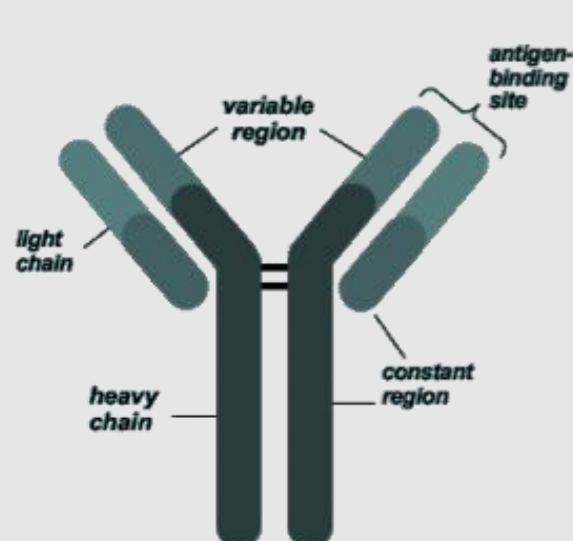
<sup>3</sup>IRCCS SAN RAFFAELE, PHARMACY, MILAN, ITALY

## Background

Nivolumab, anti-PD-1 mAb, is available as concentrated solution for IV injection and diluted in 0.9% saline. These solutions are reported to be physically and chemically stable for 24 h at 2-8 °C and 8 h at 20-25 °C. Since the “real-world” use after dilution in IV infusion bags may exceed the manufacturer’s recommendations, “in-use” studies assessing their stability is important as the formulation components are diluted and may not be able to protect the protein against degradation or denaturation.

## Aim and objectives

The aim of this study was to assess physicochemical and microbiological in-use stability of diluted solution of nivolumab stored at 2-8 °C.



pH

Osmolality

Turbidimetry

DLS

SEC-HPLC

Gel electrophoresis

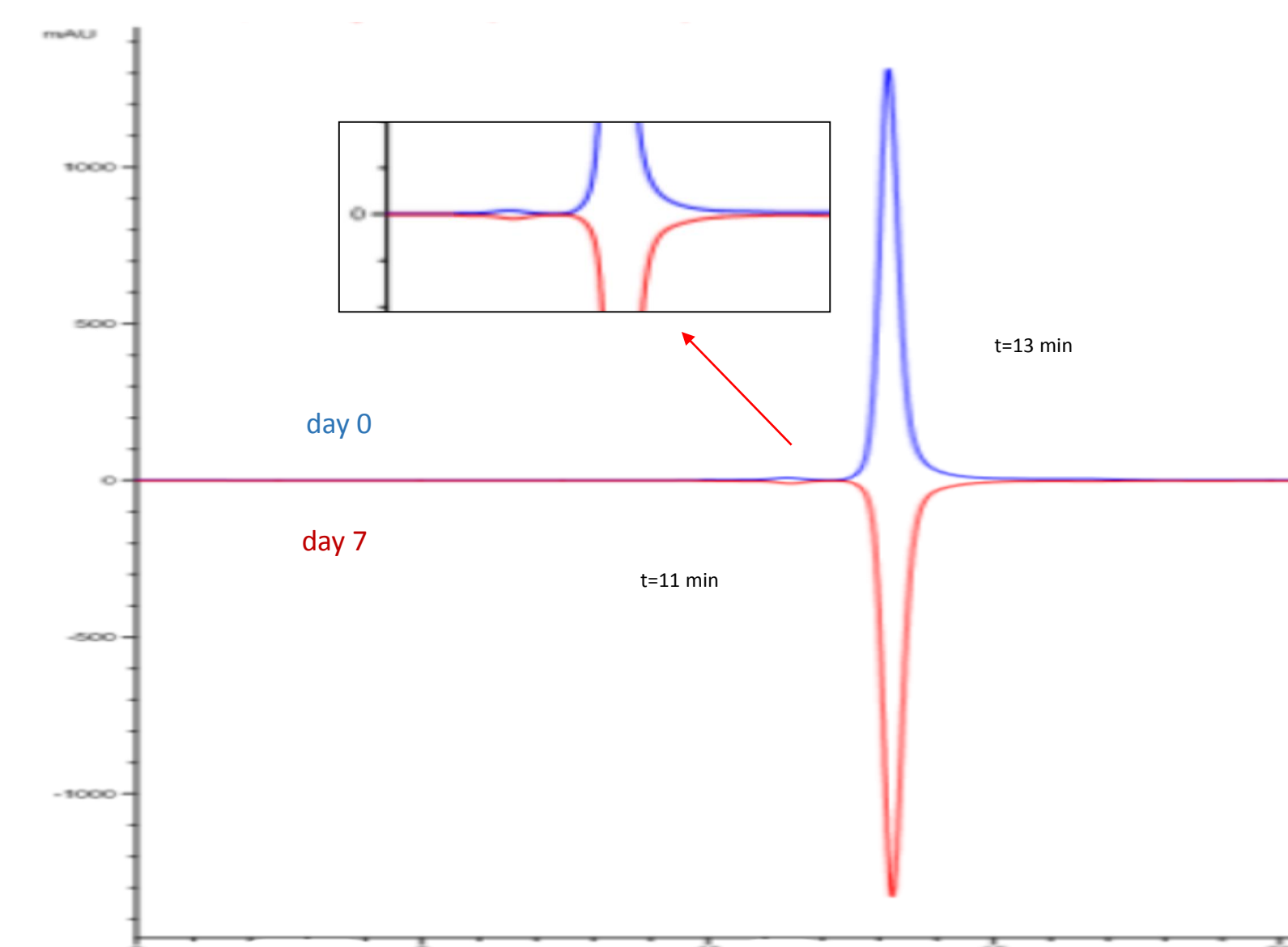
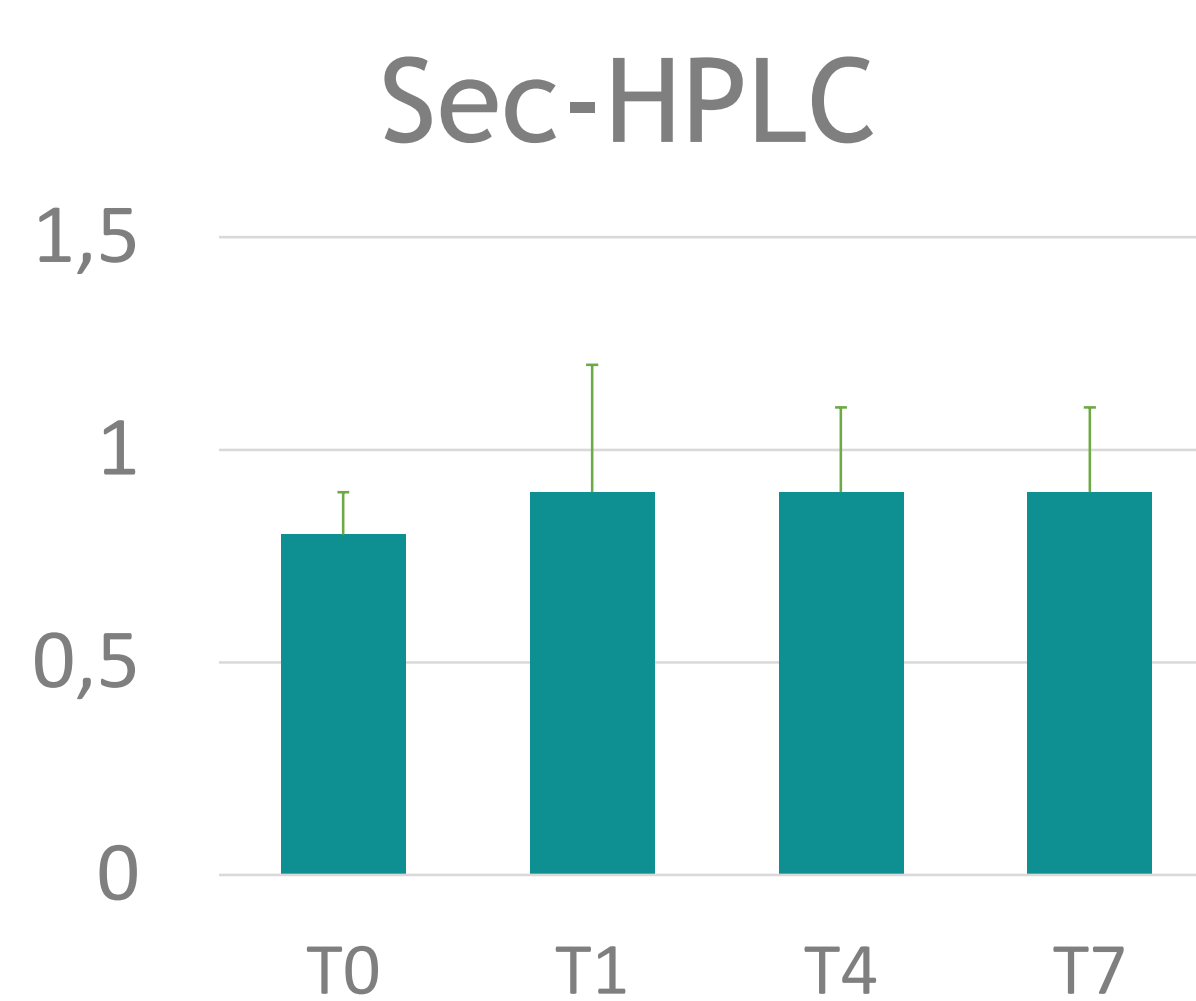
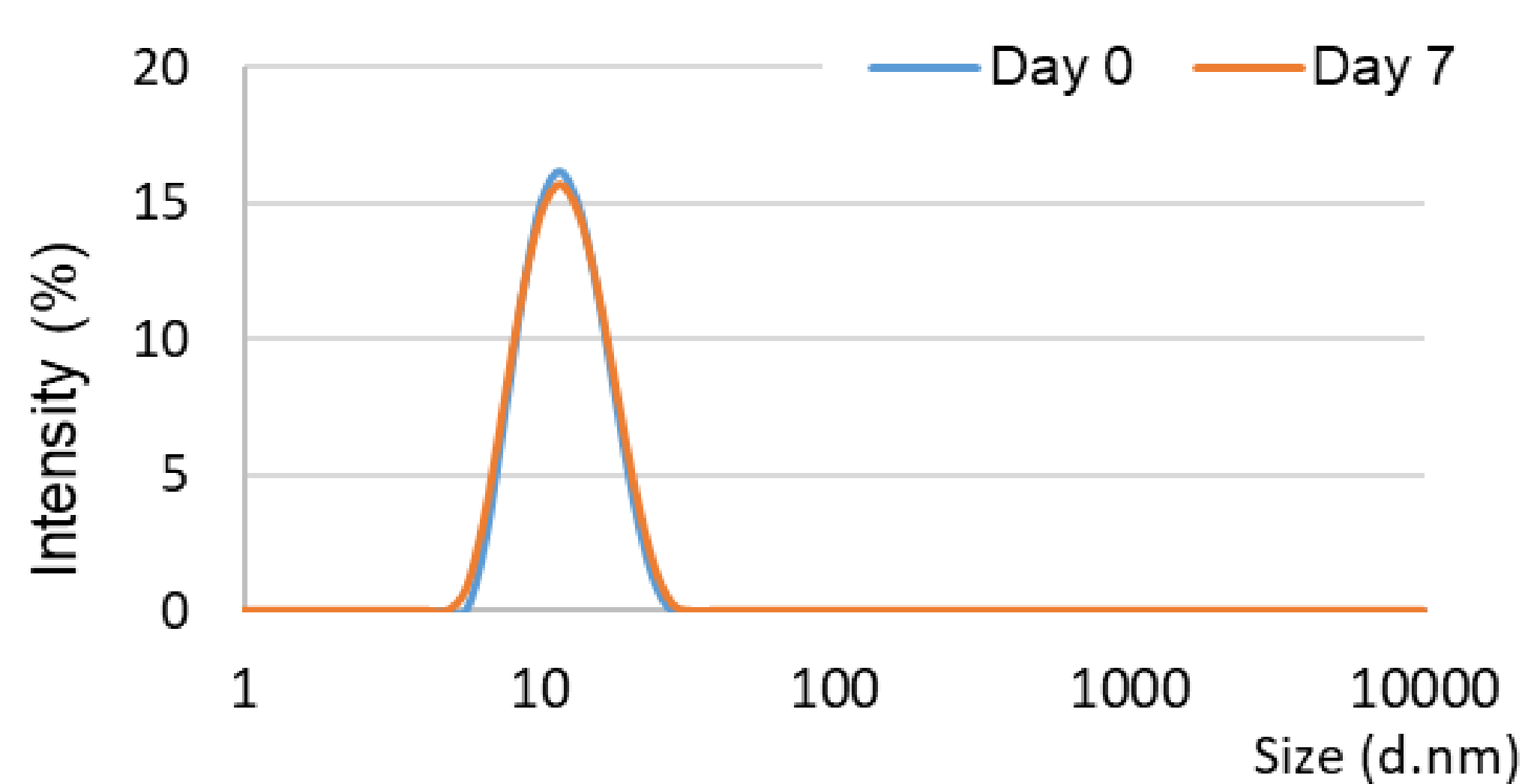
Microbiological assay

## Material and methods

Four bags of nivolumab were compounded at concentration of 2 mg/mL with 0.9% saline solution and stored at 2-8 °C over a 7-day period. At selected time points, different methods were used to evaluate stability

## Results

- ✓ Diluted nivolumab solutions remained clear and colorless
- ✓ All samples were not affected in terms of formation of sub-visible particles or changes in pH or osmolality
- ✓ Results of SEC-HPLC analyses revealed no change in high molecular weight (HMW), soluble aggregate, or low molecular weight (LMW), fragmented product.
- ✓ Relative ratio remained constant over time
- ✓ Gel electrophoresis under both no-reducing and reducing conditions detected no change in band distribution
- ✓ No bacterial or fungal contamination after 30 day of storage



## Conclusion

These analyses demonstrate that nivolumab under the dilution conditions required for IV infusion can be stored for 7 days at 2-8 °C with no evidences of physical or chemical alteration



UNIVERSITÀ  
DEGLI STUDI  
DI MILANO



3PC-019  
melania.rivano@gmail.com

