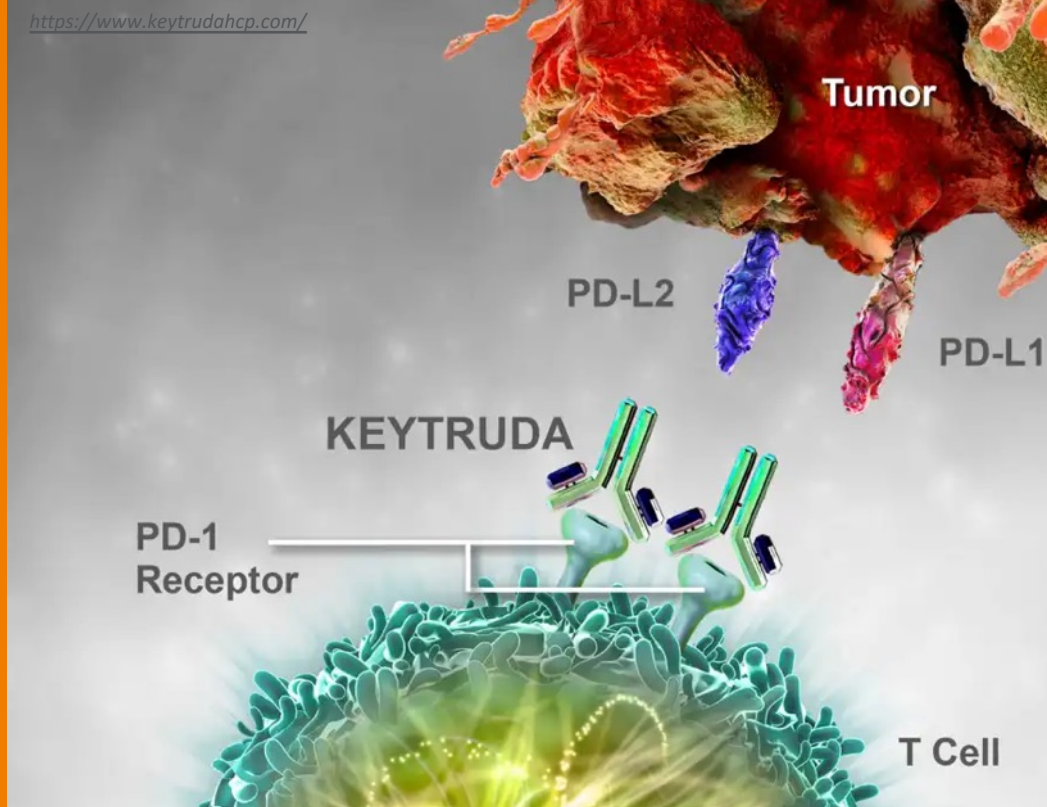


Dr Alexandre ACRAMEL

Wednesday 5th October 2022

Biological stability of Pembrolizumab after dilution and storage in 0.9% NaCl infusion polyolefin bags

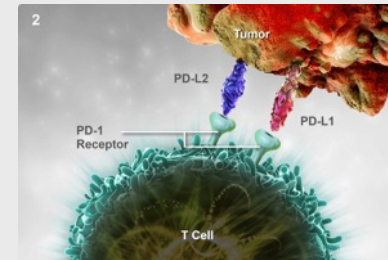
<https://www.keytrudahcp.com/>





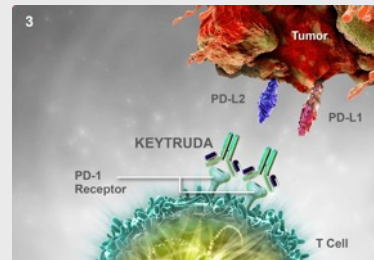
Normal immune response

When functioning properly, T cells are activated and can attack tumor cells.



Tumor evasion and T-cell de-activation

Some tumors can evade the immune system through the PD-1 pathway. The PD-L1 and PD-L2 ligands on tumors can bind with PD-1 receptors on T cells to inactivate the T cells.



T-cell reactivation with KEYTRUDA

KEYTRUDA binds to the PD-1 receptor and blocks its interaction with PD-L1 and PD-L2, which helps to restore the immune response. While having an effect on the tumor, this could also affect normal healthy cells.

<https://www.keytrudahcp.com/>



Indications:

Advanced Melanoma or Adjuvant Therapy for Melanoma; Advanced Non-Small Cell Lung Cancer; Metastatic or Unresectable, Recurrent Head and Neck Squamous Cell Carcinoma; Relapsed or Refractory Classical Hodgkin Lymphoma; Refractory or Relapsed Primary Mediastinal Large B-cell Lymphoma; Advanced Urothelial Carcinoma; High-Risk Non-muscle Invasive Bladder Cancer; Advanced MSI-H/dMMR Cancers; Advanced MSI-H/dMMR Colorectal Cancer; Advanced Gastric or GEJ Cancer; Advanced Esophageal or GEJ Carcinoma; Advanced Cervical Cancer; Advanced Hepatocellular Carcinoma; Advanced Merkel Cell Carcinoma; Adjuvant Treatment for RCC or Advanced Renal Cell Carcinoma; Advanced MSI-H/dMM; Endometrial Carcinoma; Advanced TMB-H Cancers; Advanced Cutaneous Squamous Cell Carcinoma; Advanced TNBC or High-Risk Early-Stage Triple-Negative Breast Cancer

Stability after dilution and storage: 7j 1mg/ml (NaCl 0.9%, POF), 2-8°C

Stabilité des solutions : Pembrolizumab

	Icon	Concentration	Température	Stabilité	Durée	Code
	∅	25 mg/ml	25°C	?	24	3771
POF	▲	1 mg/ml	17-23°C	☀	7	4334 A+
POF	▲	1 mg/ml	2-8°C	☀	7	4334 A+
	▲	1 >> 10 mg/ml	2-8°C	?	96	

STABILIS: <https://www.stabilis.org/Monographie.php?IdMolecule=973>



Avrillon et al. (SFPO, 2021):

- *Solutions at 1 mg/ml and 4 mg/ml could be stored for 2 weeks at 4°C and 1 week at RT without physicochemical alterations.*
- *However, only solutions at 4 mg/ml were stable after 30 days of storage at 4°C.*

➔ **Biological stability study needed**

Detection of Pembrolizumab & Fixation to PD1-expressing cells



Pembrolizumab diluted in 0.9% NaCl at 1 and 4 mg/ml in infusion polyolefin bags

ELISA test anti-pembrolizumab (commercial, Abcam)

Flow cytometry: Jurkat-PD1 cell line /secondary antibody specific for human Ig kappa.

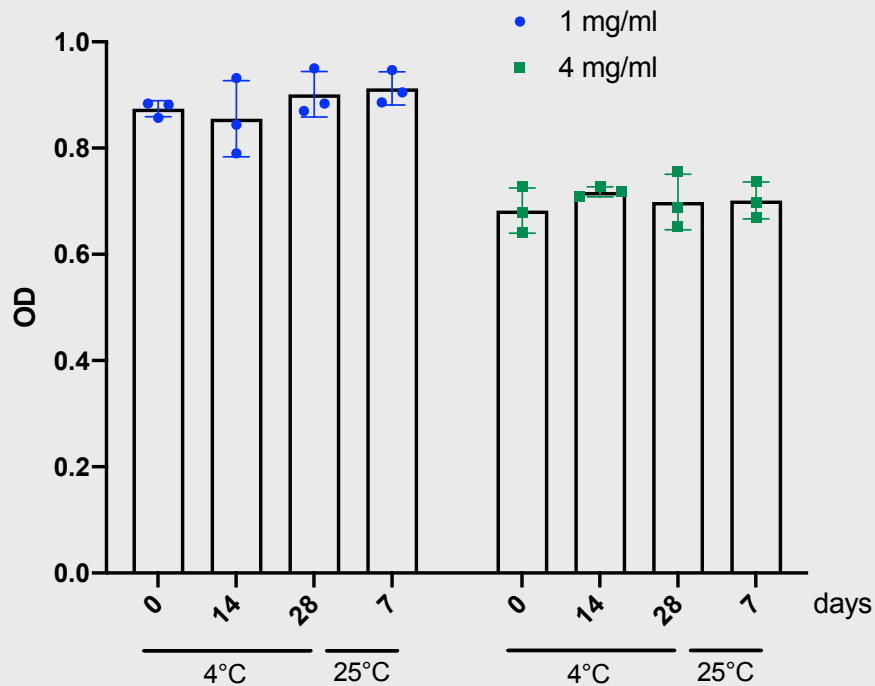
In triplicate from 3 batches of Pembrolizumab

These bags were prepared sequentially and stored at 4°C or RT. Physicochemical analyzes were carried out to ensure the compliance of these solutions



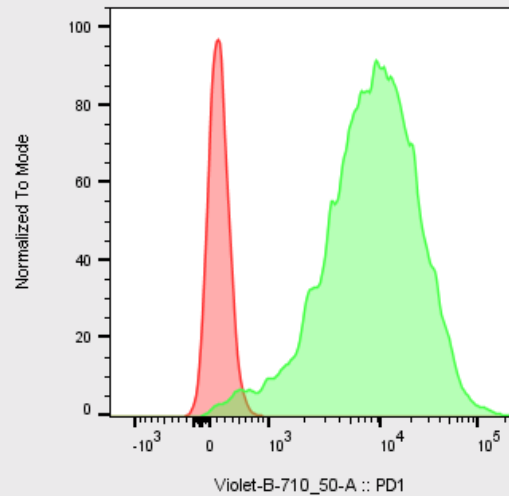
4°C: D0, D14 and D28
RT: D0 and D7

Detection of
Pembrolizumab

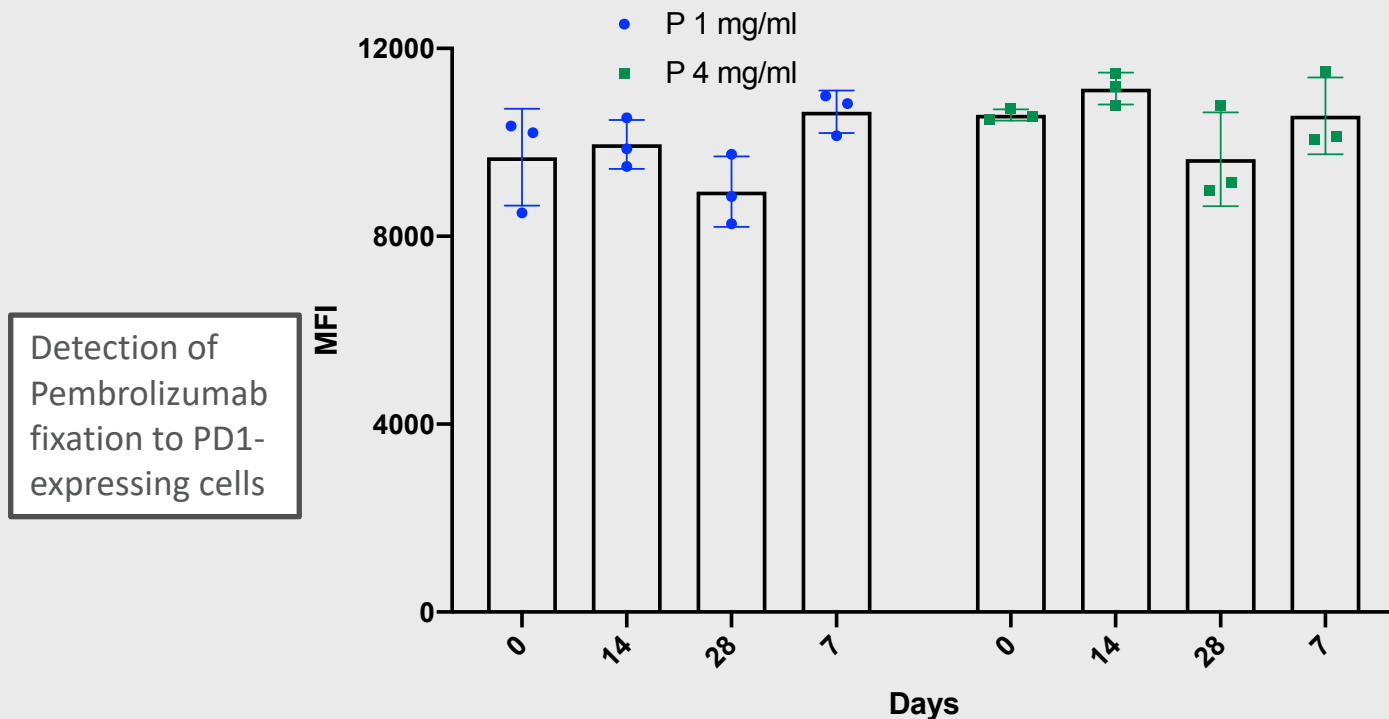


3 batches of Pembrolizumab were stored in various conditions of concentrations (1 and 4 mg/ml), temperature (4 or 25°C) and time: 14 and 28 days at 4°C and 7 days at room temperature. Then the amount of Pembrolizumab was measured in aliquots of each bag by an ELISA specific for this anti-PD-1 Ab. Individual data are representing optical density with the mean \pm SD.

PD-1 detection on Jurkat-PD1 cells



■ isotype on cells
■ Ac anti-PD1 on cells



3 batches of Pembrolizumab were stored in various conditions of concentrations (1 and 4mg/ml), temperature (4 or 25°C) and time: 14 and 28 days at 4°C and 7 days at room temperature. Then the amount of Pembrolizumab was measured in aliquots of each bag by Flow cytometry. Individual data are representing fluorescence intensity with the mean \pm SD.

The **binding capacity** of Pembrolizumab on its target is stable at **4°C for 28 days** and **7 days at room temperature (RT)** at 1 mg/ml and 4 mg/ml.

→ The mechanisms involved in the clinical effect should be conserved.

Solutions from 1 to 4 mg/ml could be stored for 2 weeks at 4°C and 1 week at RT without physicochemical and functionality alterations.

→ **The stability of preparations made in anticancer production unit could therefore be reconsidered?**

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Jurkat PD1 - Pembro

