SESION CLINICA MEDICINA INTERNA

Dra. Ana Castañón

Dra. Marina Pintor

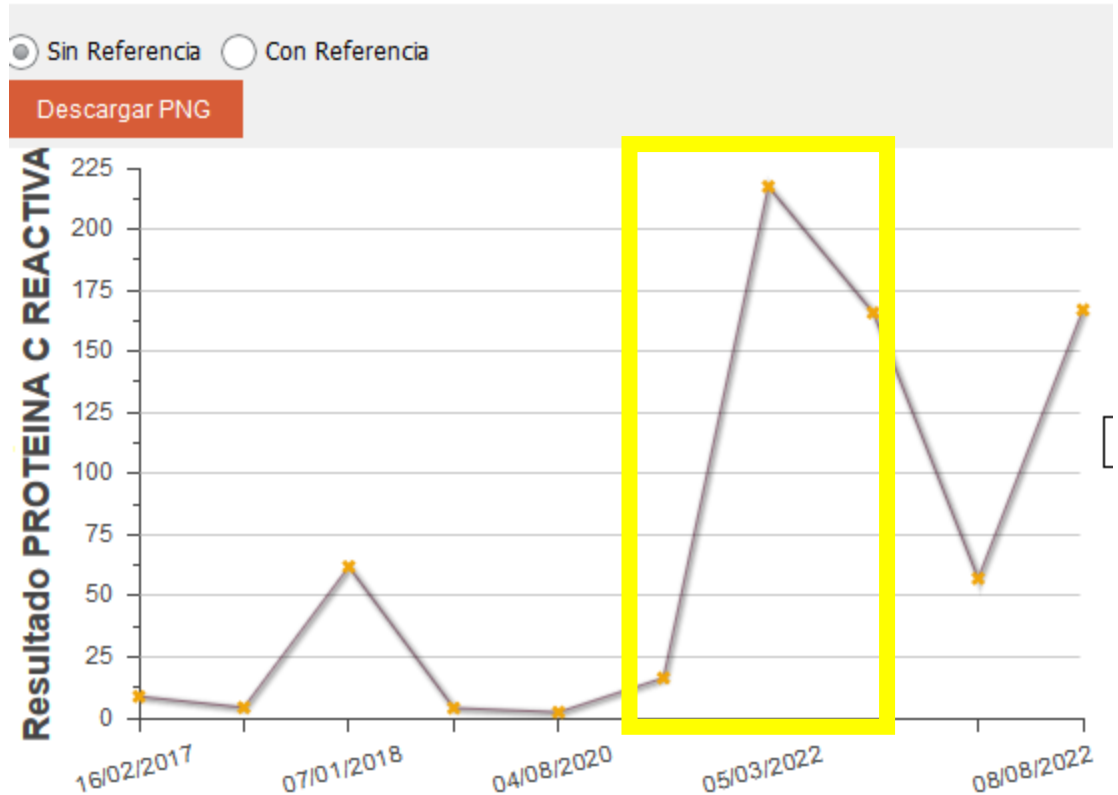
28 Septiembre 2022

Complejo Asistencial Universitario de León

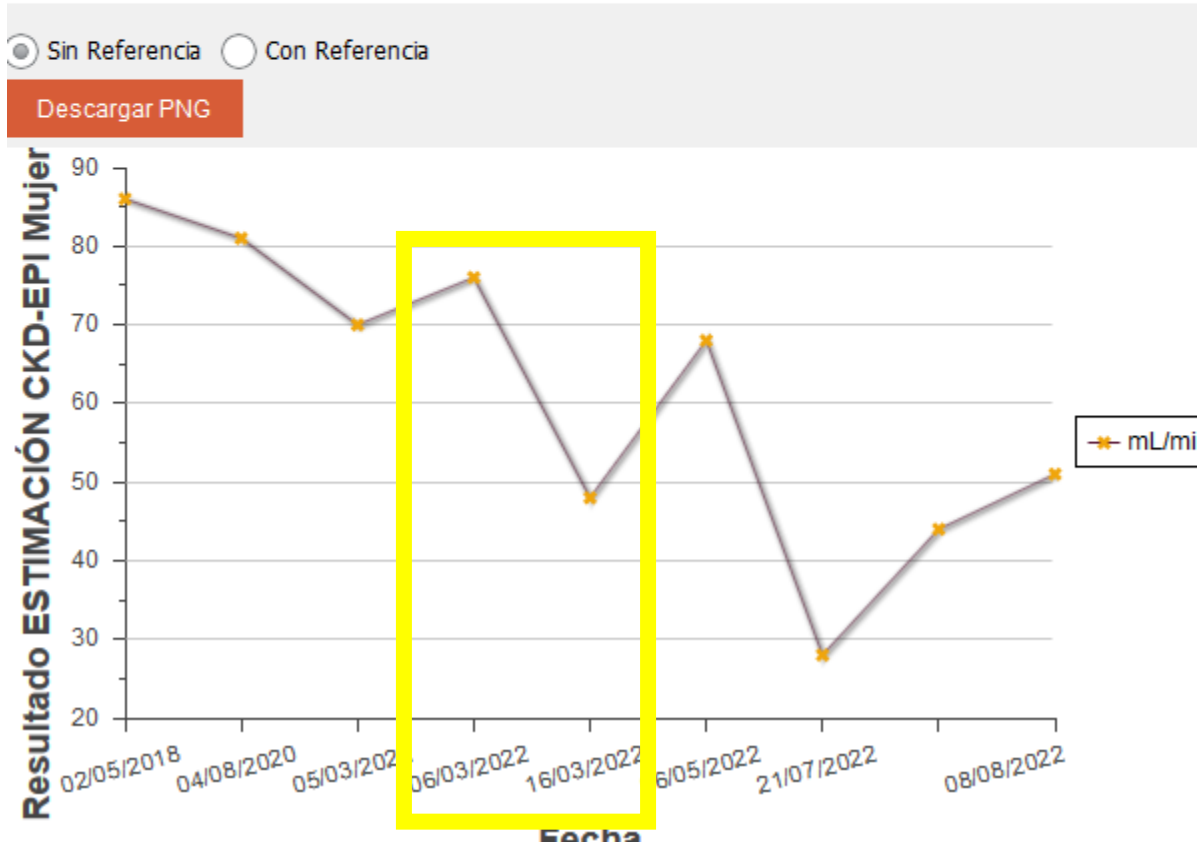
Junta de Castilla y León

Sacyl

08/01/2022 00:00:13	16.4 mg/L	[0 - 5]
05/03/2022 00:00:10	217.4 mg/L	[0 - 5]
06/03/2022 00:00:10	165.8 mg/L	[0 - 5]
21/07/2022 00:00:14	57.1 mg/L	[0 - 5]
08/08/2022 00:00:13	167.0 mg/L	[0 - 5]



05/03/2022 00:00:10	70 mL/min	[0 - 150]
06/03/2022 00:00:09	76 mL/min	[0 - 150]
16/03/2022 00:00:11	48 mL/min	[0 - 150]
06/05/2022 00:00:12	68 mL/min	[0 - 150]
21/07/2022 00:00:14	28 mL/min	[0 - 150]
22/07/2022 00:00:07	44 mL/min	[0 - 150]
08/08/2022 00:00:12	51 mL/min	[0 - 150]



Histórico PROT.TOT

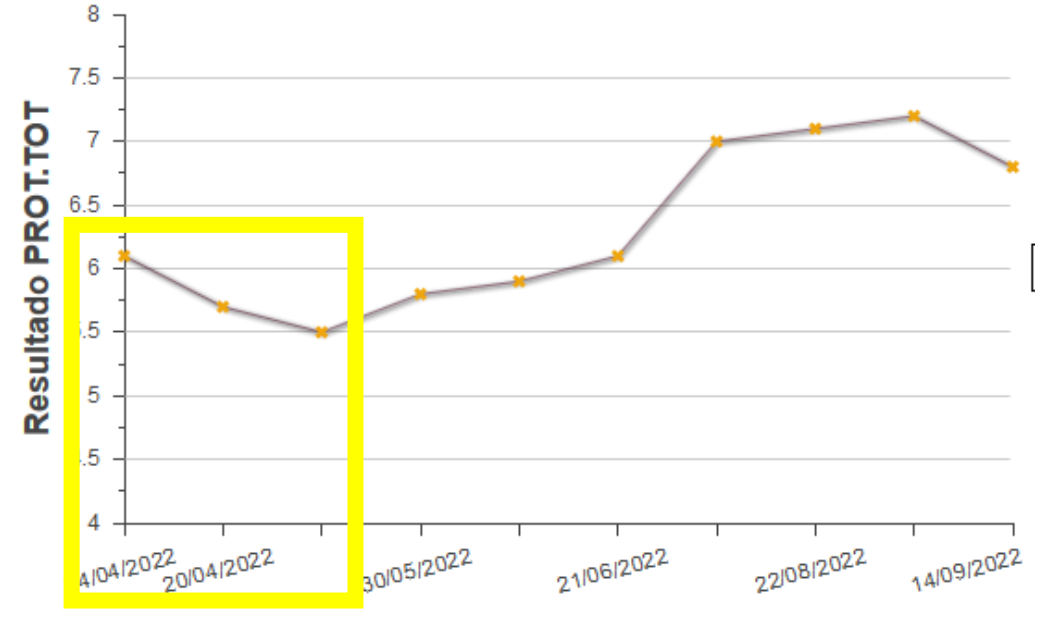
Fecha	Resultado	Val. Ref.
04/04/2022 00:00:13	6.1 g/dL	[6.4 - 8.5]
20/04/2022 00:00:09	5.7 g/dL	[6.4 - 8.5]
11/05/2022 00:00:10	5.5 g/dL	[6.4 - 8.5]
30/05/2022 00:00:11	5.8 g/dL	[6.4 - 8.5]
01/06/2022 00:00:10	5.9 g/dL	[6.4 - 8.5]
21/06/2022 00:00:12	6.1 g/dL	[6.4 - 8.5]
19/08/2022 00:00:11	7 g/dL	[6.4 - 8.5]
22/08/2022 00:00:11	7.1 g/dL	[6.4 - 8.5]
08/09/2022 00:00:10	7.2 g/dL	[6.4 - 8.5]
14/09/2022 00:00:12	6.8 g/dL	[6.4 - 8.5]

Histórico PROTEINAS ORINA 24 HORAS

Fecha	Resultado	Val. Ref.
14/03/2022 00:00:13	0.3584 g/24h	[0 - 0.15]
28/03/2022 00:00:11	2.2 g/24h	[0 - 0.15]
20/04/2022 00:00:15	3.315 g/24h	[0 - 0.15]
30/05/2022 00:00:13	3.21 g/24h	[0 - 0.15]
22/08/2022 00:00:12	1.616 g/24h	[0 - 0.15]

Sin Referencia Con Referencia

Descargar PNG

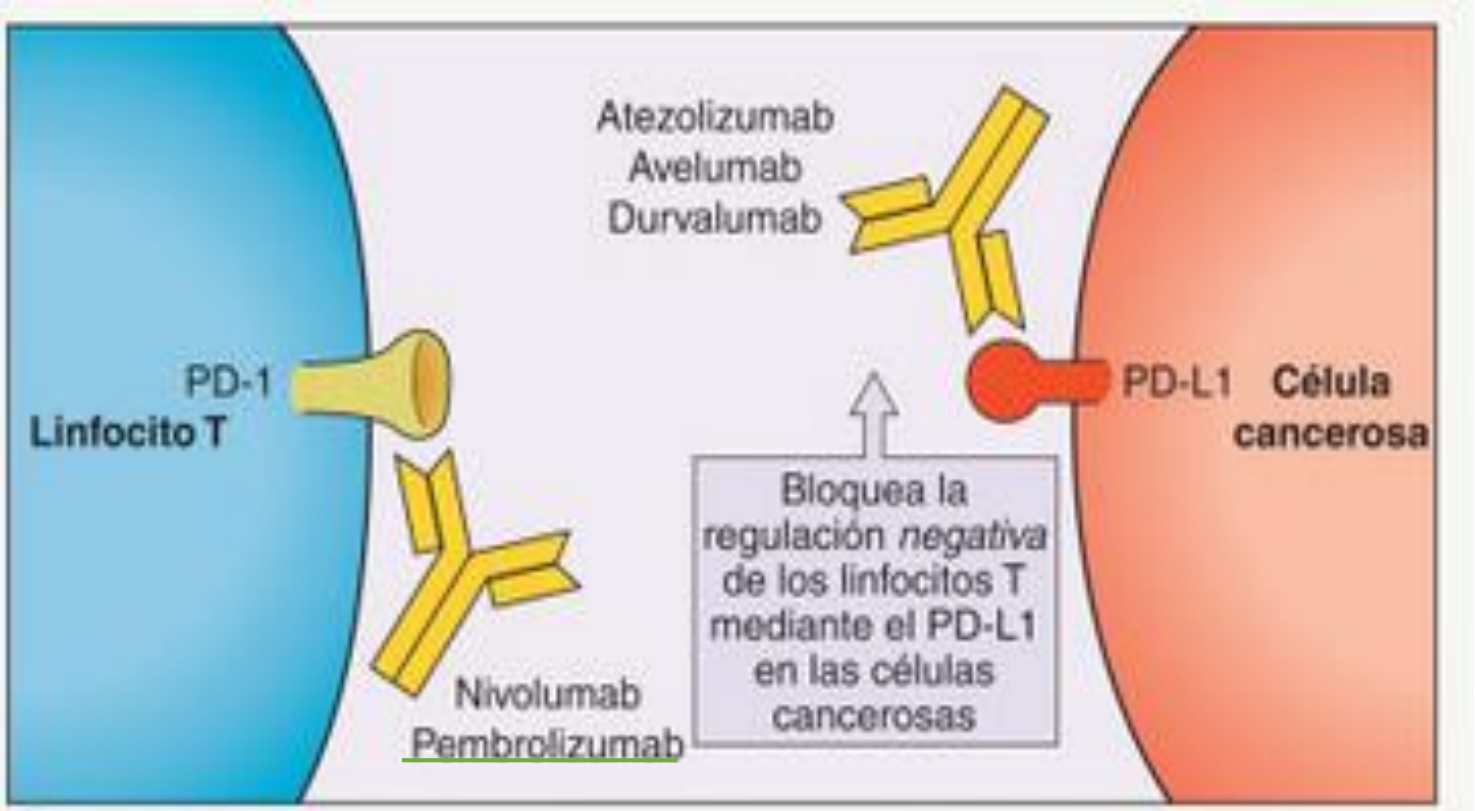


Sin Referencia Con Referencia

Descargar PNG

INMUNOTERAPIA

INHIBIDORES DEL PUNTO DE CONTROL INMUNITARIO



G Sitios de acción de los inhibidores de la proteína 1 de muerte celular programada (PD-1) y del ligando 1 de la PD (PD-L1)

PEMBROLIZUMAB

EFECTOS SECUNDARIOS

<1%:

Cardiovascular: Vasculitis

Endocrine & metabolic: Hypoparathyroidism, hypophysitis, type 1 diabetes mellitus

Gastrointestinal: Duodenitis, gastritis, increased serum amylase, increased serum lipase, pancreatitis

Hematologic & oncologic: Aplastic anemia, hemolytic anemia, immune thrombocytopenia, immunological signs and symptoms (hemophagocytic lymphohistiocytosis) (Kalmuk 2020), lymphadenitis (histiocytic necrotizing lymphadenitis [Kikuchi lymphadenitis]), sarcoidosis

Hypersensitivity: Anaphylaxis

Immunologic: Organ transplant rejection (solid)

Infection: Systemic inflammatory response syndrome

Nervous system: Demyelinating disease, encephalitis, Guillain-Barre syndrome, meningitis, myasthenia (myasthenic syndrome) (Fang 2019), myasthenia gravis (including exacerbation of myasthenia gravis), neuropathy (autoimmune), paresis (nerve)

Neuromuscular & skeletal: Myelitis, polymyalgia rheumatica, polymyositis, rhabdomyolysis

Ophthalmic: Iritis

Renal: Nephritis

NEFRITIS SECUNDARIA A INMUNOTERAPIA

Management of kidney irAEs in patients treated with immune checkpoint inhibitors*

6. Kidney toxicities

Nephritis and kidney dysfunction – diagnosis and monitoring:

- Clinical presentation and diagnosis.
- Definite ICPi-related nephritis or AKI:
  - Kidney biopsy-confirmed diagnosis compatible with ICPi nephritis or AKI, and after clinical review of risk factors.¶
- Probable ICPi-related nephritis or acute kidney failure:
  - **Both** of the following:
    - Sustained increase in serum creatinine ≥50% on at least two consecutive values or need for RRT, after clinical review of risk factors.¶
    - Absence of an alternative plausible etiology.
  - **And** at least one of the following:
    - Sterile pyuria (≥5 WBCs/hpf).
    - Concomitant or recent extrarenal irAE-eosinophilia (≥500 cells per microliter).
- Possible ICPi-related nephritis or acute kidney failure:
  - **Both** of the following:
    - Increase in serum creatinine ≥50%.
    - Need for RRT nephritis or AKI is not readily attributable to alternative causes.

Monitoring:

- Monitor patients for elevated serum creatinine before every dose.
- Routine urinalysis is not necessary, other than to rule out UTIs etc.
- For any suspected immune-mediated adverse reactions, exclude other causes (refer to below).
- For suspected kidney irAE obtain urinalysis, consider referral to nephrology.
- For patients receiving combination therapy with ICPis and other agents, assess the potential contribution of the non-iCPI treatment to the kidney failure.
- Assess for concomitant medications, prescribed and OTC, herbals, vitamins, nephrotoxic agents, or contrast media.
- If no potential alternative cause of AKI is identified, then one can assume it is ICPi-related and should forego biopsy.
- Swift treatment of autoimmune component is important.

Servicio Peticionario : **INGRESADO**

Servicio/C.Salud:**NO INFORMADO**

Cama - Habitación :

Dr./Dra :**NO INFORMADO**

Fecha solicitud **18/03/2022**

OBSERVACIONES:

PRUEBA		RESULTADO	UNIDADES	VALOR REFERENCIA
AUTOINMUNIDAD				
ANTIC CITOPLASMA NEUTROFILO		P1/2560 P-ANCA		
ANTIC DNA NATIVO		2	UI IgG/mL	[0 - 20]
MIELOPEROXIDASA	*	>134	U/ml	[0 - 5]
PROTEINASA 3		0.6	U/ml	[0 - 3]
AUTOINMUNIDAD				
screening ENAS		NEGATIVO		

Esta prueba incluye Ro,La,Sm,RNP,CENTROMERO, Scl-70,Jo-1

PEMBROLIZUMAB

EFECTOS SECUNDARIOS

<1%:

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Hypersensitivity: Anaphylaxis

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Neuromuscular & skeletal: Myelitis, polymyalgia rheumatica, polymyositis, rhabdomyolysis

Ophthalmic: Iritis

Renal: Nephritis

FICHA TECNICA

KEYTRUDA 50 mg polvo para concentrado para solución para perfusión.

Nefritis relacionada con el sistema inmunitario

Se ha notificado nefritis en pacientes que recibieron pembrolizumab (ver sección 4.8). Se debe vigilar a los pacientes en cuanto a cambios en la función renal y descartar otras causas de disfunción renal. Se deben administrar corticosteroides en caso de acontecimientos de Grado ≥ 2 (dosis inicial de 1-2 mg/kg/día de prednisona o equivalente, seguida por una reducción progresiva) y, de acuerdo con la intensidad de las elevaciones de la creatinina, pembrolizumab se debe suspender temporalmente en caso de nefritis de Grado 2 y se debe suspender definitivamente en caso de nefritis de Grado 3 o Grado 4 (ver sección 4.2).

Otras reacciones adversas relacionadas con el sistema inmunitario

En ensayos clínicos o en la experiencia tras la comercialización, se han notificado las siguientes reacciones adversas adicionales clínicamente significativas, relacionadas con el sistema inmunitario: uveítis, artritis, miositis, miocarditis, pancreatitis, síndrome de Guillain-Barré, síndrome miasténico, anemia hemolítica, sarcoidosis, encefalitis, mielitis, vasculitis, colangitis esclerosante, gastritis y cistitis no infecciosa (ver las secciones 4.2 y 4.8).

Nail toxicities are not well documented in clinical trials, and their incidence is unknown. Onycholysis (picture 9), onychoschizia (picture 10), and inflammatory nail changes may occur in th course of ICI therapy as isolated manifestations or may be associated with inflammatory dermatoses, such as psoriasis, or lichen planus [2,19,56,62-64]. Onychodystrophy has been reported ir patients who developed alopecia areata or dermatomyositis [56,65,66].

Rare cutaneous adverse events — Rarely reported cutaneous irAEs include:

- **Severe cutaneous adverse reactions** – Severe cutaneous adverse reactions, including Stevens-Johnson syndrome/toxic epidermal necrolysis (SJS/TEN) [67], acute generalized exanthematous pustulosis (AGEP) [68], and drug reaction with eosinophilia and systemic symptoms (DRESS), have been described in isolated case reports [67,69,70]. These reactions are rare, and their frequency is not yet available, although it is estimated to be less than 1 percent of all cutaneous irAEs. (See "Stevens-Johnson syndrome and toxic epidermal necrolysis: Pathogenesis, clinical manifestations, and diagnosis" and "Drug reaction with eosinophilia and systemic symptoms (DRESS)".)

- **Keratoacanthoma** – Keratoacanthoma-type squamous cell carcinoma has been reported in at least six patients with eruptive or reactive morphologies all on anti-PD-1 monotherapy (picture 11). They were treated conservatively with cryotherapy, intralesional steroids, electrodessication and curettage, and excision [71-75].

- **Autoimmune rheumatic disease** [76,77]:

  - Systemic lupus erythematosus, subacute cutaneous lupus, and bullous lupus have all been reported with anti-PD-1 monotherapy and ICI combination therapy [78-83]. (See "Drug-induced lupus".)

  - Dermatomyositis (picture 12A-B), Sjögren syndrome, systemic sclerosis, and scleroderma-like cutaneous changes have also been reported [66,84-87]. Differentiating drug-induced dermatomyositis from paraneoplastic dermatomyositis can be difficult [72,88]. (See "Malignancy in dermatomyositis and polymyositis".)

- **Vasculitis** – Vasculitis most commonly presents as large-vessel vasculitis and, less commonly, leukocytoclastic vasculitis or granulomatous polyangiitis [89-92].

- **Neutrophilic dermatoses** – Neutrophilic dermatoses, including Sweet syndrome, pustular eruptions, and pyoderma gangrenosum (picture 13), have been rarely reported [93]. Additionally, a case of pyoderma gangrenosum exacerbated by anti-PD-1 therapy was reported [94].

- **Erythema nodosum** – Erythema nodosum-like panniculitis (picture 14) has been reported in a few patients [95,96].

From: Vasculitis associated with immune checkpoint inhibitors—a systematic review

Cancer type	Age (years)	Sex	Disease	Vessel size	Immunotherapy drug	Immune checkpoint inhibited	Onset after initiation of therapy	Immune-related adverse events treatment	Cancer and immune-related adverse events outcomes	Reference
Melanoma	U	U	Autoimmune vasculitis	U	Ipilimumab	CTLA-4	U	U	U	Hersh et al. (2010) [8]
Melanoma	77	F	Lymphocytic vasculitis involving uterine and ovarian vessels	Medium vessel	Ipilimumab	CTLA-4	15 weeks	U	U	Minor et al. (2013) [9]
Melanoma	62	M	GCA	Large vessel	Ipilimumab	CTLA-4	6 months	Discontinued ipilimumab. Prednisone 50 mg daily for 3 weeks	Metastatic melanoma progressed and patient died 6 months later.	Goldstein et al. (2014) [10]
Melanoma	36	F	Retinal vasculitis	Small vessel	Pembrolizumab	PD-1	10 months	Prednisolone eye drops	Initial progression of the melanoma then remission. The patient improved post-vitrectomy with a visual acuity of 20/20	Manusow et al. (2014) [11]
Melanoma	U	U	Large vessel vasculitis	Large vessel	Pembrolizumab	PD-1	4 weeks	U	U	Pinkston et al. (2016) [12]
Mesothelioma	31	M	Isolated vasculitis of the peripheral nervous system	Medium vessel	Nivolumab	PD-1	3 months	Discontinued nivolumab. Methyl-prednisolone 1000 mg IV daily for 5 days	U	Liao et al. (2016) [13]
Melanoma	53	F	Isolated vasculitic neuropathy (polyneuropathy with endoneural vasculitis)	Medium vessel	Pembrolizumab	PD-1	3 weeks	Methylprednisolone 500 mg IV daily for 3 days then oral prednisone 50 mg daily for 6 weeks then tapered over 6 months until 5 mg daily and then discontinued	Remission	Aya et al. (2016) [14]
Melanoma	56	F	GPA	Small vessel	Pembrolizumab	PD-1	1 week	Cyclophosphamide 150 mg oral daily and methylprednisolone IV	U	Van Den Brom et al. (2016) [15]
Melanoma	U	U	PACNS	Single organ	Pembrolizumab	PD-1	U	U	U	Bender et al. (2016) [16]
Melanoma	51	F	PACNS	Single organ	Pembrolizumab	PD-1	18 months	Methylprednisolone 2 mg/kg IV daily	U	Khoja et al. (2016) [17]

Histórico MIELOPEROXIDASA

Fecha	Resultado	Val. Ref.
24/03/2022 00:00:13	>134 U/ml	[0 - 5]
08/06/2022 00:00:13	20 U/ml	[0 - 5]
31/08/2022 00:00:13	15 U/ml	[0 - 5]
20/09/2022 00:00:12	6.7 U/ml	[0 - 5]

Sin Referencia Con Referencia

Descargar PNG