

# A Study on Dermatomyositis and the Relation to Malignancy

ANDREEA DANIELA TUDORANCEA<sup>1</sup>, PAULINA LUCIA CIUREA<sup>1</sup>,  
ANANU FLORENTIN VREJU<sup>1</sup>, ADINA TURCU-STIOLICA<sup>2</sup>,  
CRISTINA ELENA GOFITA<sup>1</sup>, CRISTINA CRIVEANU<sup>1</sup>,  
ANCA EMANUELA MUSETESCU<sup>1</sup>, STEFAN CRISTIAN DINESCU<sup>1</sup>

<sup>1</sup>Department of Rheumatology, University of Medicine and Pharmacy of Craiova, Romania

<sup>2</sup>Department of Pharmacoconomics, University of Medicine and Pharmacy of Craiova, Romania

**ABSTRACT:** The idiopathic inflammatory myopathies (IIM) are a group of heterogeneous systemic diseases which include as main subtypes: polymyositis (PM), dermatomyositis (DM) and inclusion body myositis (IBM). The key feature of IIMs is the muscle weakness, accompanied by a characteristic skin rash in DM patients. The overall risk for malignancy in IIM is higher compared to the age-and sex-matched general population. Most epidemiologic studies have included only PM and DM patients and reported consistently higher rates of malignancy in DM. Most common types of cancer in DM are adenocarcinoma of the lung, ovary or gastrointestinal tract, melanoma and non-Hodgkins lymphoma. The highest risk for malignancy is seen in the first year after DM diagnosis. Multiple disease features have been linked to the development of cancer in DM. These include: older age, male sex, skin necrosis, Gottron sign, heliotrope rash, dysphagia, low complement C4, lymphocytosis, poor response to corticosteroids and rapid disease progression. Our study included 23 patients with DM, divided into two groups based on the association of malignancy, in order to compare clinical and demographic features, laboratory markers and analyze characteristic of cancer development.

**KEYWORDS:** Dermatomyositis, malignancy, idiopathic inflammatory myopathy, paraneoplastic syndrome.

## Introduction

The idiopathic inflammatory myopathies (IIM) are a group of heterogeneous systemic diseases which include as main subtypes: polymyositis (PM), dermatomyositis (DM) and inclusion body myositis (IBM).

The key feature of IIMs is the muscle weakness and this is accompanied by a characteristic skin rash in DM patients.

The overall risk for malignancy in IIM is higher compared to the age-and sex-matched general population.

Most epidemiologic studies have included only PM and DM patients and reported consistently higher rates of malignancy in DM [1].

Furthermore, an increased malignancy-related mortality ratio is observed in DM patients as compared with the general population [2].

The incidence of malignancy is significantly higher in the first year since diagnosis and is generally associated with older age.

The type of malignancy differs with sex and ethnicity.

In studies from western countries, the most common types of cancer in DM are adenocarcinoma of the lung, ovary or

gastrointestinal tract, melanoma and non-Hodgkins lymphoma [3,4].

In many Asian countries, nasopharyngeal cancer is the predominant type of cancer associated with DM [5,6].

Patients' survival rates can be markedly improved through early identification of cancer-associated IIM.

Our study included 23 patients with DM, divided into two groups based on the association of malignancy, in order to compare demographic and clinical features, laboratory markers and analyze characteristic of cancer development.

## Material and Methods

This was a retrospective study of patients admitted to the Rheumatology Department of the Emergency County Hospital in Craiova.

Patient files were selected based on diagnosis of dermatomyositis.

A total of 23 patients were included in the study and divided into two subgroups, 10 patients with cancer and 13 patients without cancer.

Variables used for statistical analysis included age, sex, serum markers, disease history, prevalence of certain clinical features and temporal relation between DM and cancer development.

The study was approved by the Hospital Ethics Committee with the number of 37802/September 7th, 2021.

Mann-Whitney U test was used in order to determine statistical differences in the laboratory assessment.

The results were expressed as mean±standard deviation and median (interquartile range) for continuous variables, and as percentages for categorical variables.

A p-value less than 0.05 was considered as statistically significant.

Statistical association of gender was examined with Fisher's Exact test. Statistical

analysis was performed using GraphPad Prism 9.1.2 software for Microsoft Windows, GraphPad Software, San Diego, CA, USA.

## Results

Twenty-three consecutive patients diagnosed with dermatomyositis in the last two years were enrolled in this study: 10 with cancer and 13 without cancer.

Study arms were statistically similar for age, gender, as in Table 1, but there was a tendency for malignant disease in older patients, (57.50±7.75 vs. 54.69±7.02, p-value=0.669).

**Table 1. Sociodemographic and clinical characteristics of the two groups of patients.**

Characteristics Mean±standard deviation Median (IQR)	Cancer arm (N=10)	Non-cancer arm (N=13)	p-value
Age	57.50±7.75 57 (54.5-61)	54.69±7.02 55 (49.5-60.5)	0.376
Gender			0.669
Female	7 (70%)	7 (54%)	
Male	3 (30%)	6 (46%)	
Disease duration	3.88±4.33 1.75 (0.42-8.5)	2.32±2.83 0.5 (0.42-5.5)	0.446
Glutamic oxaloacetic transaminase (GOT) (U/l)	58.90±20.79 55 (45-71.5)	64.46±46.82 45 (27-92.5)	0.693
GPT	55.10±14.38 57.5 (48.8-62)	54.08±29.21 45 (28-90)	0.605
Creatine kinase (U/l)	575.30±463.87 483.5 (186.3-968.8)	600.77±363.81 560 (250-925)	0.522
Lactate dehydrogenase (U/l)	434.60±267.15 385 (200-583.5)	388.15±174.37 450 (218-545)	0.738
C-reactive protein (mg/l)	15.73±12.20 10.7 (5.8-27.7)	24.15±22.61 15 (6.5-51)	0.446
ESR erythrocyte sedimentation rate (mm/h)	46.20±26.50 35 (25-66.3)	62.46±33.22 60 (30.5-100)	0.166
Fibrinogen	469.80±101.89 482 (350-557.3)	465.38±154.95 500 (285-590)	0.879
Hemoglobin (g/dl)	11.70±0.71 11.8 (11-12.1)	11.69±1.25 12 (10.5-12.5)	0.976
Hematocrit	39.04±1.93 39.4 (38-40.3)	39.08±0.86 39 (38-40)	0.879
Leucocytes	6734±837.46 6500 (5950-7425)	6227.69±835.57 5900 (5600-6530)	0.208
Thrombocytes	227100±56392.38 238500 (178750-253750)	211615.38±50381.11 189000 (162000-257500)	0.879
Rheumatoid factor	7.18±7.91 4.4 (0-15.25)	8.77±5.21 10 (5-12)	0.832
DXA	-2.72±0.31 -2.85 (-2.9-2.58)	-0.82±1.31 0 (-2.25-0)	0.005

No predilection was found between male or female gender for patients with or without cancer, even if the percentage of female with cancer was greater than the percentage of female without cancer.

On the cancer arm, patients had a longer mean duration of myositis, but without statistical significance (p-value=0.446).

CK level is the same between the two groups (p-value=0.522), with elevated values in both groups.

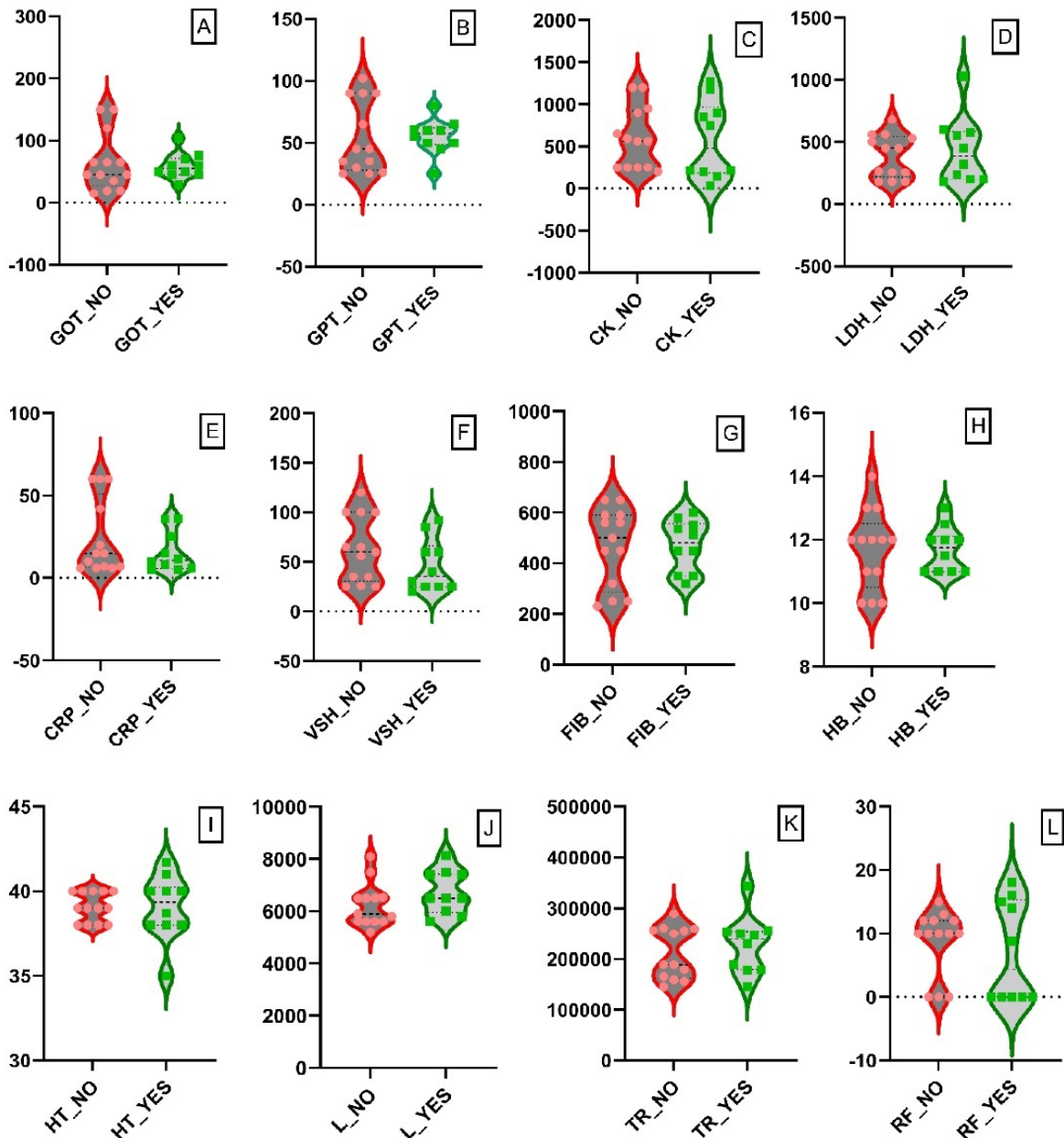
The degree of CK elevation does not correlate with the presence of cancer among patients.

Another elevated muscle enzyme, lactate dehydrogenase (LDH) was the same between cancer and non-cancer patients.

The serum inflammatory biomarkers ESR and CRP were increased, but without differences between patients.

There were no significant differences in the levels of fibrinogen, hemoglobin, hematocrit, leucocytes, thrombocytes and rheumatoid factor between cancer and non-cancer patients with dermatomyositis.

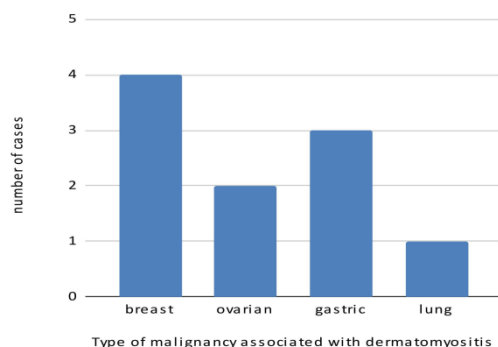
The mean value for dual-energy X-ray absorptiometry (DXA) was significant lower in the cancer group than in non-cancer patients (p-value=0.005) (see Figure 1).



**Figure 1. Comparison of serum markers between dermatomyositis patients with and without cancer.**  
 A) GOT, glutamic oxaloacetic transaminase; B) GPT, glutamic-pyruvic transaminase; C) CK, creatine kinase;  
 D) LDH, Lactate dehydrogenase; E) CRP, C-reactive protein; F) VSH, erythrocyte sedimentation rate;  
 G) FIB, Fibrinogen; H) HB, Hemoglobin; I) HT, Hematocrit; J) L, Leucocytes; K) TR, Thrombocytes;  
 L) RF, Rheumatoid factor; M) DXA, dual-energy X-ray absorptiometry.

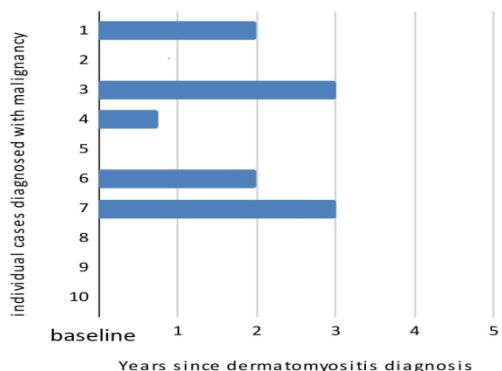
The data from the group of patients with dermatomyositis and malignancy was further analyzed for prevalence of certain clinical features and temporal relation between myositis and cancer development.

The most prevalent form of malignancy was breast cancer, observed in 4/10 patients (Figure 2).



**Figure 2. Type of malignancy associated with dermatomyositis.**

Half of the patients were diagnosed with cancer at baseline with an additional one within the first year and all forms of cancer developed within the first 3 years from myositis diagnosis (Figure 3).



**Figure 3. Temporal relation between diagnosis of dermatomyositis and malignancy.**

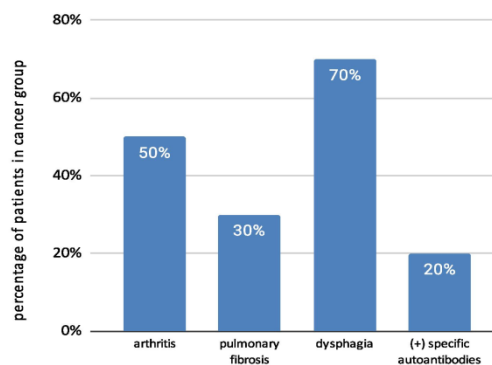
Dysphagia, a well-known risk factor for malignancy was observed in 70% of patients in the cancer group; this was more prevalent compared to patients in the non-cancer group, where dysphagia was reported in 47% of cases (8/23), but without statistical significance (p-value=0.11).

Arthritis, defined as joint pain not-related to degenerative disease, was present in half of the patients with malignancy, similarly to non-cancer group (50% vs. 65%, p value=0.49).

Pulmonary fibrosis and positivity for myositis-specific antibodies were each detected

in only 2 cases of myositis associated with malignancy (Figure 4).

These two features were more prevalent in the non-cancer group, where 47% of patients displayed pulmonary fibrosis (p value=0.20) and 65% were positive for either anti-Mi2 or anti-Jo1 antibodies (p value=0.04).



**Figure 4. Prevalence of clinical and serologic features in patients which developed cancer.**

## Discussion

The idiopathic inflammatory myopathy defines a group of diseases characterized by symmetric proximal muscle weakness as the most recognizable common clinical feature.

Polymyositis and dermatomyositis are the main clinical forms and have been more extensively studied.

This group also includes inclusion body myositis and the more recently added immune-mediated necrotizing myopathy.

Epidemiologic studies of IIMs have reported an incidence of 1.16 to 19/million/year and prevalence ranging from 2.4 to 33.8 per 100 000 inhabitants [7].

The overall female to male ratio is 2 to 3:1.

DM has a bimodal age distribution, with the first peak between 5 to 15 years and the other at 45 to 60 years.

Poor prognostic factors in myositis which are related to lower rate of response and higher mortality include: advanced age, African American race, interstitial lung disease, positive anti-SRP antibodies, dysphagia, dysphonia, cardiac involvement and associated malignancy.

Patients with DM have a 4.5-fold higher risk of developing malignancy than the general population [8].

Incidence of malignancy in DM patients is reported between 8.6-32% in western countries and 3.8-24.4% in Asian countries [9].

The 5-year survival rate in DM patients with cancer is 10-56%, significantly lower compared to overall DM patients, of 60-90.1% [9,10].

The mortality rate of patients with DM and cancer ranges from 16-75% and is mostly due to cancer than myositis.

Malignancy is usually detected in a more advanced stage in this setting [11].

Risk for malignancy is not restricted only to older age, as shown in a study by Chen et al, too, which reported a 7.86 standardized incidence ratio for cancer in DM patients younger than 20 years [12].

The precise mechanism behind the association of malignancy and myositis is not clear.

Some studies demonstrated that muscle inflammation will improve after the malignancy is treated successfully and in this setting myositis is considered a paraneoplastic phenomenon [8].

However, DM can develop at the same time as, before, or after the diagnosis of cancer.

The relation can be directed in both ways; both diseases could contribute to the development of the other.

Some explanations rely on the potential effect of immunosuppressive therapy in DM, an immunologic response through expression of autoantigens or increased vigilance for cancer screening in DM patients [9,13].

In studies from European countries, the most common types of cancer associated with DM were ovarian, lung, gastric, colorectal cancer, pancreatic and non-Hodgkin lymphoma.

Adenocarcinoma is the most common pathological type [9,14].

By contrast, nasopharyngeal malignancy was the most frequent type of cancer in a study based in Taiwan [12].

In most studies, the highest risk for malignancy is seen in the first year after DM diagnosis.

We observed similar results, with 6 out of 10 patients being diagnosed with malignancy at the same time with DM diagnosis or within one year.

Liu et al. reported data from 239 DM patients, of which 17.9% developed cancer.

In 69.7% of cases, cancer diagnosis occurred within 1 year before or after DM diagnosis, while only 4.6% of cases developed cancer after 5 years [9].

In a meta-analysis from Canada, the standardized incidence ratio for malignancy was 17.29 in the first year, 2.7 from 2-5 years, and 1.37 after 5 years [15].

Nevertheless, there is a persistent elevated risk for cancer over time, and this calls for close surveillance not only at the time of diagnosis.

Older age is a well-known independent risk factor for malignancy.

This is defined in most studies as over 45 years.

In addition, multiple disease features have been linked to the development of cancer in DM. These include: male sex, skin necrosis, Gottron sign, heliotrope rash, dysphagia, low albumin, low complement C4, lymphocytosis, poor response to corticosteroids and rapid disease progression [9].

In our study, dysphagia was the most prevalent risk factor, present in 7/10 patients. Interestingly, some studies observed a relation between low levels of CPK and cancer risk [16].

Other clinical features have been negatively associated with malignancy.

These protective factors include joint pain, interstitial lung disease, positive anti-Jo1 antibodies and Raynaud's phenomenon [8,9].

Finally, antibody expression can help predict the risk for cancer development.

Studies consistently observed that positive anti-TIF1- $\gamma$  antibodies are associated with cancer risk.

Anti-TIF1- $\gamma$  antibodies are detected in 50-100% of patients with cancer associated myositis [9].

Trallero-Araguas et al quantified the usefulness of anti-p155 (TIF- $\gamma$ ) antibody screening and established that positive testing to p155 had a 27.28 higher association with cancer compared to p155-negative patients [17].

By contrast, anti-MDA5 antibodies are considered protective for malignancy.

Anti-NXP2 antibodies have also been correlated with cancer risk [18], but results are not consistent between studies [9].

## Conclusion

Dermatomyositis has an increased risk for malignancy, superior than other forms of idiopathic inflammatory myopathies.

Every patient should be thoroughly examined at diagnosis for risk factors and undergo appropriate screening at baseline and follow-up if needed.

Most cases develop cancer in the first year after diagnosis, although a high risk persists even after 5 years.

Cancer screening is recommended even at younger ages followed by long-term surveillance.

## Acknowledgements

None

## Conflict of Interest

None to declare.

## References

1. Lu X, Yang H, Shu X, Chen F, Zhang Y, Zhang S, et al. Factors Predicting Malignancy in Patients with Polymyositis and Dermatomyositis: A Systematic Review and Meta-Analysis. *PLoS One*, 2014, 8;9(4):e94128.
2. Qiang JK, Kim WB, Baibergenova A, Alhusayen R. Risk of Malignancy in Dermatomyositis and Polymyositis: A Systematic Review and Meta-Analysis. *J Cutan Med Surg*, 2016, 17, 21(2):131-136.
3. Zahr ZA, Baer AN. Malignancy in myositis. *Curr Rheumatol Rep*, 2011, 13(3):208-215.
4. Jouary T, Gracia C, Lalanne N, Vital A, Taieb A, Delaunay M. Rapidly lethal dermatomyositis associated with metastatic melanoma. *J Eur Acad Dermatol Venereol*, 2008, 22(3):399-401.
5. Aggarwal R, Oddis C V. Paraneoplastic myalgias and myositis. *Rheum Dis Clin*, 2011, 37(4):607-621.
6. Teoh JW, Yunus RM, Hassan F, Ghazali N, Abidin ZAZ. Nasopharyngeal carcinoma in dermatomyositis patients: A 10-year retrospective review in Hospital Selayang, Malaysia. *Reports Pract Oncol Radiother J Gt Cancer Cent Pozn Polish Soc Radiat Oncol*, 2014, 19(5):332-336.
7. Meyer A, Meyer N, Schaeffer M, Gottenberg J-E, Geny B, Sibilia J. Incidence and prevalence of inflammatory myopathies: a systematic review. *Rheumatology (Oxford)*, 2015, 54(1):50-63.
8. Yang Z, Lin F, Qin B, Liang Y, Zhong R. Polymyositis/dermatomyositis and Malignancy Risk: A Metaanalysis Study. *J Rheumatol*, 2015, 42(2):282-291.
9. Liu Y, Xu L, Wu H, Zhao N, Tang Y, Li X, et al. Characteristics and predictors of malignancy in dermatomyositis: Analysis of 239 patients from northern China. *Oncol Lett*, 2018, 16(5):5960-5968.
10. Dankó K, Panyi A, Constantin T, Borgulya G, Szegedi G. Long-term survival of patients with idiopathic inflammatory myopathies according to clinical features: a longitudinal study of 162 cases. *Medicine (Baltimore)*, 2004, 83(1):35-42.
11. Mebazâa A, Boussen H, Nouira R, Rokbani L, Ben Osman-Dhahri A, Bouaouina N, et al. Dermatomyositis and malignancy in Tunisia: a multicenter national retrospective study of 20 cases. *J Am Acad Dermatol*, 2003, 48(4):530-534.
12. Chen Y-J, Wu C-Y, Huang Y-L, Wang C-B, Shen J-L, Chang Y-T. Cancer risks of dermatomyositis and polymyositis: a nationwide cohort study in Taiwan. *Arthritis Res Ther*, 2010, 12(2):R70.
13. Casciola-Rosen L, Nagaraju K, Plotz P, Wang K, Levine S, Gabrielson E, et al. Enhanced autoantigen expression in regenerating muscle cells in idiopathic inflammatory myopathy. *J Exp Med*, 2005, 201(4):591-601.
14. Hill CL, Zhang Y, Sigurgeirsson B, Pukkala E, Mellemkjaer L, Airio A, et al. Frequency of specific cancer types in dermatomyositis and polymyositis: a population-based study. *Lancet*, 2001, 357(9250):96-100.
15. Qiang JK, Kim WB, Baibergenova A, Alhusayen R. Risk of Malignancy in Dermatomyositis and Polymyositis. *J Cutan Med Surg*, 2017, 21(2):131-136.
16. András C, Panyi A, Constantin T, Csiki Z, Szekanecz E, Szodoray P, et al. Dermatomyositis and polymyositis associated with malignancy: a 21-year retrospective study. *J Rheumatol*, 2008, 35(3):438-444.
17. Trallero-Araguás E, Rodrigo-Pendás JÁ, Selva-O'Callaghan A, Martínez-Gómez X, Bosch X, Labrador-Horrillo M, et al. Usefulness of anti-p155 autoantibody for diagnosing cancer-associated dermatomyositis: A systematic review and meta-analysis. *Arthritis Rheum*, 2012, 64(2):523-532.
18. Fiorentino DF, Chung LS, Christopher-Stine L, Zaba L, Li S, Mammen AL, et al. Most patients with cancer-associated dermatomyositis have antibodies to nuclear matrix protein NXP-2 or transcription intermediary factor 1 $\gamma$ . *Arthritis Rheum*, 2013, 65(11):2954-2962.

---

*Corresponding Author: Florentin Ananu Vreju, Department of Rheumatology, University of Medicine and Pharmacy Craiova, Romania, 2 Petru Rareș Street, Postal code: 200349, Craiova, Romania, e-mail: florentin.vreju@umfcv.ro*