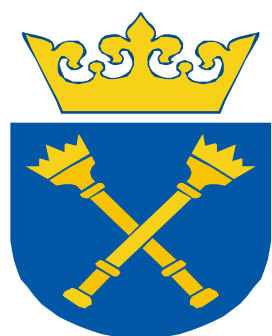


# Primary and secondary plasma cell leukemia - prognostic indicators

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Kazimierz Dolny nad Wisłą, May 11 2018



# Plasma cell leukemia

Plasma cell leukemia (PCL) is a rare and aggressive disease associated with malignant proliferation of plasma cells (PCs)

Diagnostic criteria of PCL based on quantity of PCs:

- absolute number  $>2 \times 10^9/l$  OR
- $>20\%$  of the total leucocyte count

PCL can develop:

- *de novo* (primary PCL, pPCL); 60% of all cases
- transformation of myeloma (secondary PCL, sPCL); 40% of all cases

# Poor prognosis of pPCL

	N	Median OS [months]
Noel & Kyle, 1989	25	6.8
Dimopoulos MA et al. 1994	12	12
García-Sanz R. et al. 1999	26	8
Tiedemann RE et al. 2008	39	11
Colović M, et al. 2008	30	4.5
Peijing Q. et al. 2009	24	14
Pagano L. et al. 2011	76	12.6

The survival of patients with pPCL was short

Noel P, Kyle RA. *Am J Med.* 1987;83:1062-1068. US  
Dimopoulos MA et al. *Br J Haematol.* 1994;88:754-759.  
García-Sanz R, et al. *Blood.* 1999;93:1032-1037.  
Tiedemann RE et al. *Leukemia.* 2008;22:1044-1052.

Colović M, et al. *Med Oncol.* 2008;25:154-160.  
Peijing Q. et al. *Acta Haematol.* 2009;121:47-51.  
Pagano L. et al. *Ann Oncol.* 2011;22:1628-1635.

# Poor prognosis of sPCL

	N	Median OS [months]
Noel & Kyle, 1989	18	1.3
Tiedemann RE et al. 2008	41	1.3
Pagano L. et al. 2011	9	2

The survival of patients with sPCL was extremely poor

Noel P, Kyle RA. *Am J Med.* 1987;83:1062-1068. US  
Tiedemann RE et al. *Leukemia.* 2008;22:1044-1052.  
Pagano L. et al. *Ann Oncol.* 2011;22:1628-1635

# PCL in the era of novel agents

Retrospective medical records review  
in 34 participating institutions from 3 continents  
All patients diagnosed with PCL  
between 2006 and 2016

117 pts.  
with pPCL

101 pts.  
with sPCL

71% ← diagnosed in the current decade → 85%

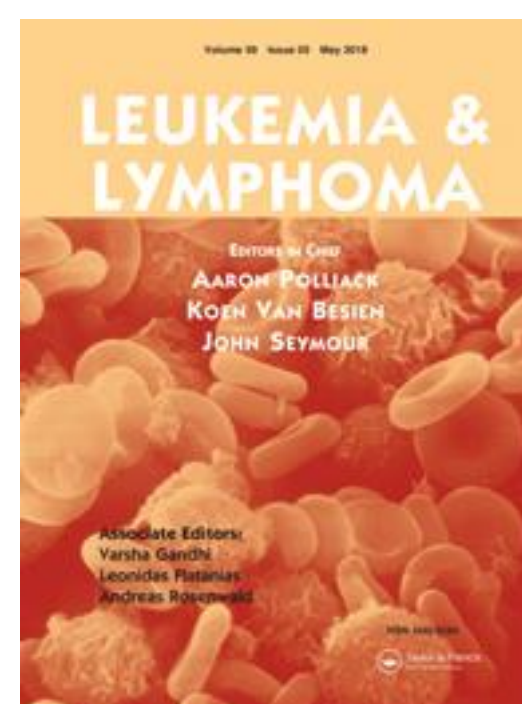
## Prognostic indicators in primary plasma cell leukaemia: a multicentre retrospective study of 117 patients

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We report a multicentre retrospective study that analysed clinical characteristics and outcomes in 117 patients with primary plasma cell leukaemia (pPCL) treated at the participating institutions between January 2006 and December 2016. The median age at the time of pPCL diagnosis was 61 years. Ninety-eight patients were treated with novel agents, with an overall response rate of 78%. Fifty-five patients (64%) patients underwent upfront autologous stem cell transplantation (ASCT). The median follow-up time was 50 months (95% confidence interval [CI] 33; 76), with a median overall survival (OS) for the entire group of 23 months (95% CI 15; 34). The median OS time in patients who underwent upfront ASCT was 35 months (95% CI 24-3; 46) as compared to 13 months (95% CI 6-3; 35-8) in patients who did not receive ASCT ( $P = 0.001$ ). Multivariate analyses identified age  $\geq 60$  years, platelet count  $\leq 100 \times 10^9/l$  and peripheral blood plasma cell count  $\geq 20 \times 10^9/l$  as independent predictors of worse survival. The median OS in patients with 0, 1 or 2-3 of these risk factors was 46, 27 and 12 months, respectively ( $P < 0.001$ ). Our findings support the use of novel agents and ASCT as frontline treatment in patients with pPCL. The constructed prognostic score should be independently validated.

**Keywords:** myeloma, plasma cell leukaemia, therapeutic response, survival, prognosis.



## Secondary plasma cell leukemia: a multicenter retrospective study of 101 patients

Journal:	<i>Leukemia and Lymphoma</i>
Manuscript ID:	GLAL-2018-0020.R1
Manuscript Type:	Original Article – Clinical
Date Submitted by the Author:	11-Apr-2018
Complete List of Authors:	Jurczynski, Artur; Jagiellonian University Medical College, Hematology Department Castillo, Jorge Avivi, Irit Czepiel, Jacek; Uniwersytet Jagiellonski w Krakowie Davila, Julio Vij, Ravi Fiala, Mark; Washington University School of Medicine, Division of Oncology Gozzetti, Alessandro; Azienda Ospedaliera Universitaria Senese Grzasko, Norbert; St. John's Cancer Center, Department of Hematology; Uniwersytet Medyczny w Lublinie, Department of Hematooncology and Bone Marrow Transplantation Milunovic, Vitor Hus, Iwona; Uniwersytet Medyczny w Lublinie Mądry, Krzysztof; Warszawski Uniwersytet Medyczny Waszczuk-Gajda, Anna; Warszawski Uniwersytet Medyczny Usnarska-Zubkiewicz, Lidia Dębski, Jakub; Uniwersytet Medyczny im Piastow Slaskich we Wroclawiu Atilla, Erden; Ankara University, Department of Hematology Beksac, Meral; Ankara University Medical School Mele, Giuseppe; Antonio Perrino Hospital, Haematology and BMT Unit Sawicki, Wlademar; Military Medical Institute, Hematology Department Jayabalan, David Charliński, Grzegorz; Medical University of Warsaw Gyula Szabo, Agoston Hajek, Roman; Faculty Hospital FN, Brno and University of Ostrava School of Medicine, Delforge, Michel; University Hospital Leuven, Kopacz, Agnieszka; Oncology Center, Municipal Hospital Fantl, Dorotea; Waage, Anders; Norwegian University of Technology & Science, Cruseo, Edvan; Santa Casa Medical School, Sao Paolo Hungria, Vania Richardson, Paul; Harvard, Hematology and Oncology Laubach, Jacob; Dana Farber Cancer Institute, Medical Oncology Guerrero-Garcia, Thomas; Dana Farber Cancer Institute Liu, Jieqi Vesole, David; John Theurer Cancer Center at Hackensack University Medical Center,

# Characteristics of pts. with pPCL

Characteristic	pPCL, n=117
Age $\geq$ 60 years	55%
Males	40%
HGB $\leq$ 10 g/dl	80%
WBC $>$ 15 x 10 <sup>9</sup> /l	52%
PLT $\leq$ 100 x 10 <sup>9</sup> /l	49%
LDH $\uparrow\uparrow\uparrow$	67%
IgG	45%
Light chain only	30%
IgA	15%

Percentages of non-missing observations

# Characteristics of pts. with sPCL

Characteristic	sPCL, n=101
Time from MM diagnosis	31 months
Males	45%
ASCT in MM treatment	55%
WBC > 15 x 10 <sup>9</sup> /l	15%
PLT ≤100 x 10 <sup>9</sup> /l	79%
LDH ↑↑↑	80%
IgG	50%
Light chain only	15%
IgA	35%

Percentages of non-missing observations

# Cytogenetic risk

Cytogenetic abnormality	pPCL	sPCL <sup>a</sup>
CD38/CD138	100%	100%
CD56	52%	71%
t(11;14)	20%	19%
del(17p)	34%	46%
complex <sup>b</sup>	22%	5%

Percentages of positive results in patients tested

<sup>a</sup> - tested at sPCL diagnosis

<sup>b</sup> -  $\geq 3$  cytogenetic abnormalities

# Therapy and response

Overall response rate depending on different treatment use

Treatment	pPCL, n/N (%)	sPCL, n/N (%)
ChemoTx	6/8 (75%)	6/17 (35%)
PI only	4/7 (57%)	3/4 (75%)
IMiD only	2/2 (100%)	0/1 (0%)
ChemoTx + PI	38/48 (79%)	16/26 (61%)
ChemoTx + IMiD	12/17 (70%)	3/11 (27%)
PI + IMiD	12/15 (80%)	2/6 (33%)
ChemoTx + PI + IMiD	9/9 (100%)	4/6 (66%)
MonoTx	12/17 (70%)	9/23 (39%)
DoubleTx	62/80 (77%)	21/43 (49%)
TripleTx	9/9 (100%)	4/6 (66%)
Upfront ASCT	42/50 (84%)	13/14 (93%)

n – pts. with CR or VGPR or PR, N – all pts. using treatment

# How do novel treatments change pPCL outcomes?

Small sample & heterogeneity limited possibility to estimate effects of agents separately

Longer 1-year and 2-years OS of pts. treated with **tripleTx** suggests that outcomes can be better than when using single or two agents

	n	median follow-up	median OS [months]	1-year OS	2-years OS
MonoTx	17	108	27	77%	58%
DoubleTx	80	51	23	69%	46%
<b>TripleTx</b>	9	13	NA	<b>89%</b>	<b>71%</b>

After upfront **ASCT** 78% of pPCL patients showed at least PR, with a median OS of 23 months following induction

# How do novel treatments change sPCL outcomes?

Small sample & heterogeneity limited possibility to estimate effects of agents separately  
ORR rates were increasing with number of different agents in combination

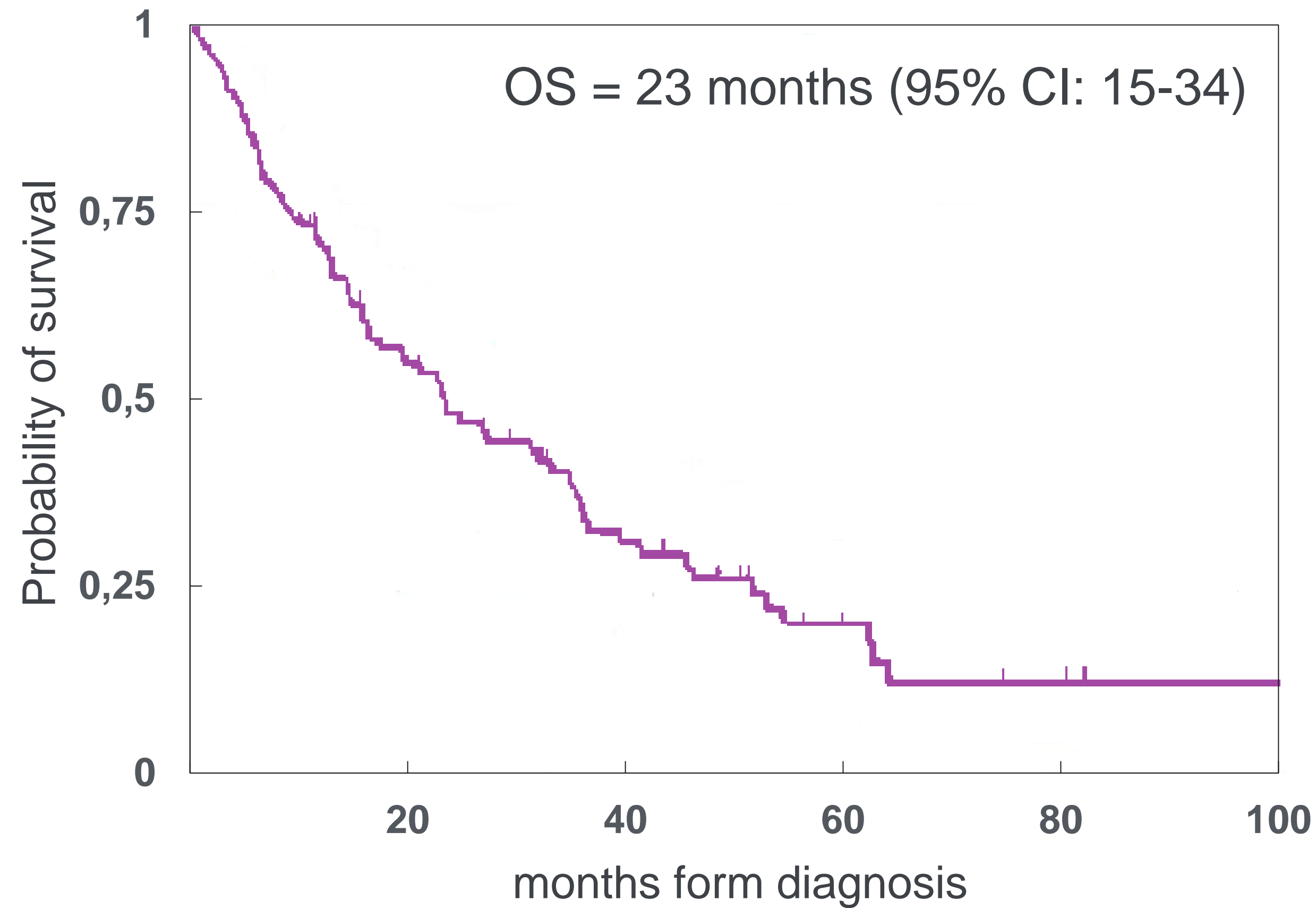
	n	ORR
MonoTx	23	39%
DoubleTx	43	49%
TripleTx	7	66%

PI presence in the treatment protocol also increased ORR

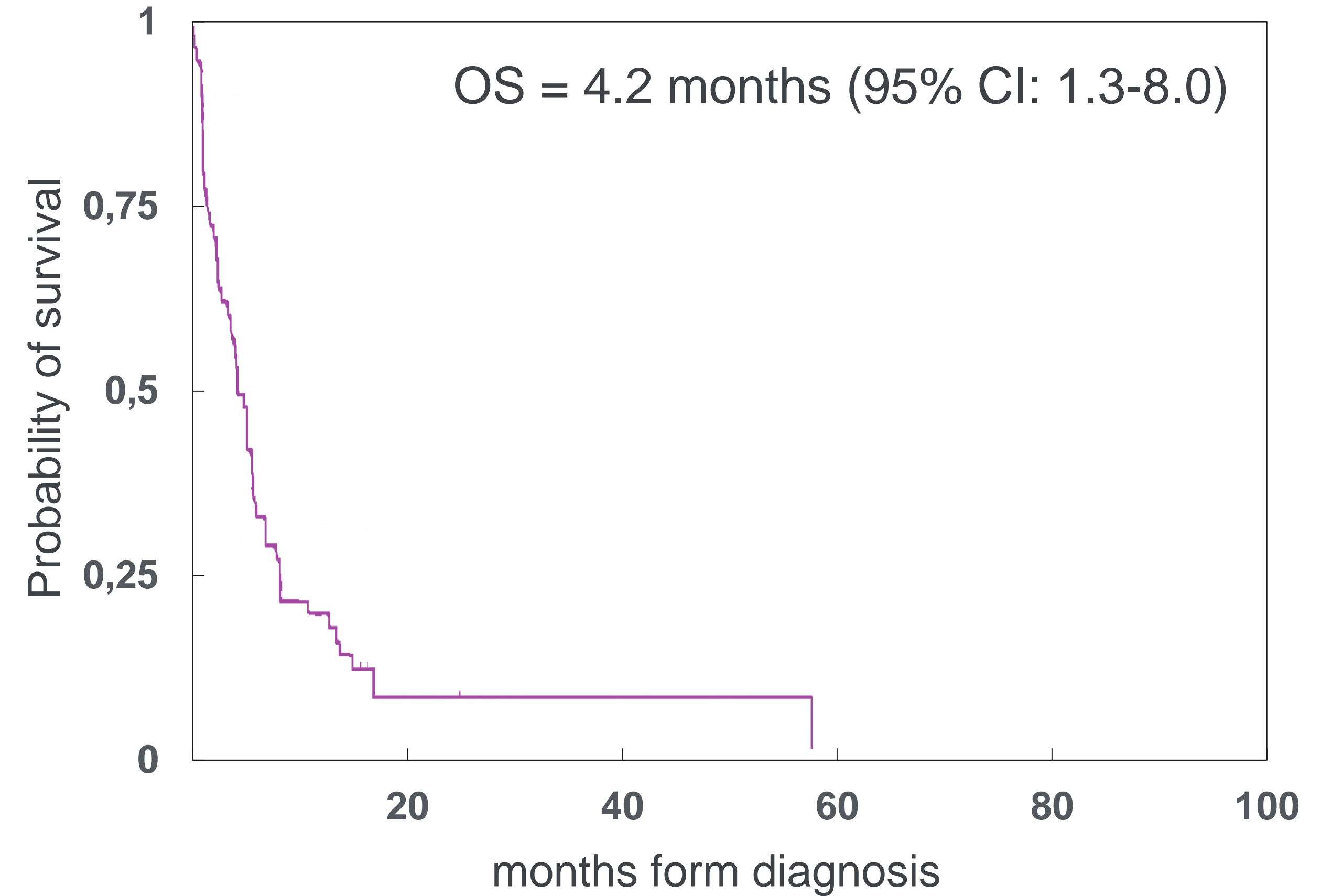
	n	ORR
PI-based regimen	42	59%
other regimen	30	30%

# Survival

## pPCL



## sPCL



# Predictors of survival

## pPCL<sup>a</sup>

Median OS [months]	Median OS [months]	HR (95% CI) <sup>b</sup>
Age ≤ 60 years 36	Age ≥ 60 years 16	2.3 (1.4-3.8)
PLT > 100 x 10 <sup>9</sup> /l 34	PLT ≤ 100 x 10 <sup>9</sup> /l 16	2.1 (1.3-3.4)
PCs ≥ 20 x 10 <sup>9</sup> /l 31	PCs ≥ 20 x 10 <sup>9</sup> /l 19	1.9 (1.0-3.7)

## sPCL

Median OS [months]	Median OS [months]	HR (95% CI) <sup>b</sup>
PLT > 100 x 10 <sup>9</sup> /l 3.5	PLT ≤ 100 x 10 <sup>9</sup> /l 13.2	4.0 (2.0-8.0)

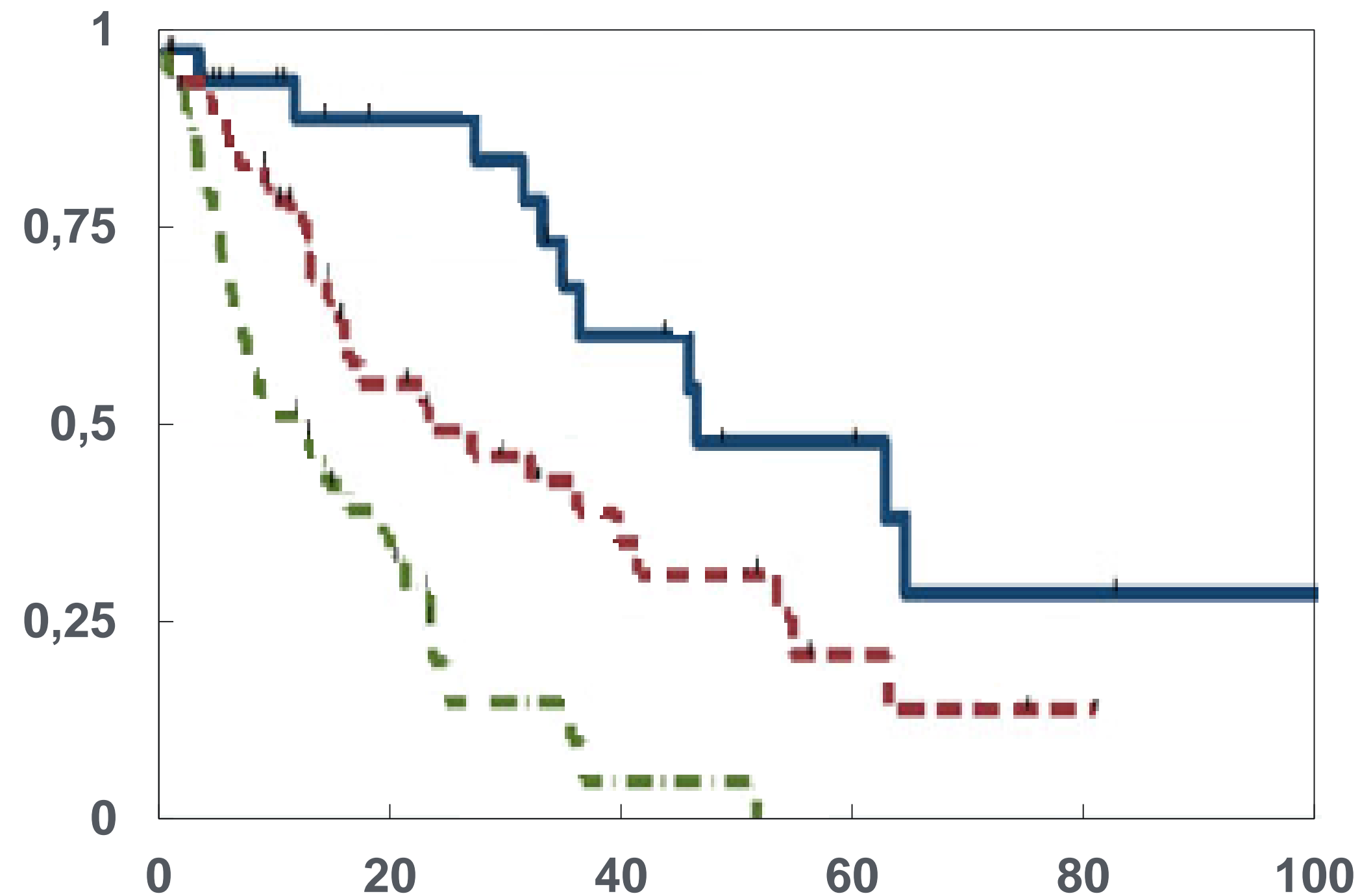


Predictors of shorter survival

a – CD56 expression was also the predictor of shorter survival in pts. with pPCL, but expression status was available in less than 50% of pts.  
b – univariate analysis

# Risk staging in pPCL

Independent predictors of worse OS, had similar HRs and were used to develop a **pPCL Prognostic Index** (PCL-PI) by assigning 1 point per adverse prognostic factor. PCL-PI value ranges from 0 to 3.



- PCL-PI = 0, (n=26), median OS = 46 mths.
- - - PCL-PI = 1, (n=51), median OS = 17 mths.
- - - PCL-PI = 2-3, (n=51), median OS = 12 mths.

PCL-PI: 0 vs. 1, HR: 2.2 (95% CI: 1.1 – 4.4),  $p = 0.03$

PCL-PI: 0 vs. 2-3, HR: 5.8 (95% CI: 2.8 – 12.0),  $p < 0.001$



# PCL-PI

## clinical implications

### Advantages of PCL-PI:

- variables included in the index can be easily determined at the time of diagnosis
- it enables to identify a subset of patients who may particularly benefit from more intensive therapy



# Summary

## pPCL

- Prognosis could be improved with the implementation of novel therapies, such as PI, IMiD, as well as ASCT
- PCL-PI may support treatment planning and requires validation in next studies

## sPCL

- sPCL prognosis remains poor
- patients may benefit from implementation of salvage multidrug PI-based regimens and ASCT
- nevertheless, novel agents with higher efficacy are needed.



# Studies limitations

- Retrospective character of collected data
- Lack of standardization
- Samples heterogeneity and small size
- Incompleteness of clinical and laboratory data (e.g. cytogenetics)
- No patients which were frail and did not obtain treatment

Oddział Krakowski Polskiego Towarzystwa Hematologów i Transfuzjologów  
Katedra i Klinika Hematologii Collegium Medicum UJ w Krakowie  
**FUNDACJA CENTRUM LECZENIA SZPICZAKA**



zapraszają do GALERII ANNA w Krakowie przy ulicy Szpitalnej 17  
[www.galeriaanna.pl](http://www.galeriaanna.pl)

w dniu **29 MAJA 2018 roku** (wtorek) o godz. 16.00

na I spotkanie **GRUPY WSPARCIA** PACJENTÓW i ICH  
RODZIN ze SZPICZAKIEM PLAZMOCYTOWYM

prof. dr hab. med. Aleksander B. Skotnicki,  
dr hab. med. Artur Jurczyszyn,  
mgr Iwona Pieniążek – **Słowo wstępne**

lek. Anna Suska – **Epidemiologia i etiopatogeneza  
szpiczaka plazmocytozy (10 minut)**

mgr Olga Czerwińska-Ledwig – **Badanie poziomu kinezyfobii  
i jej przyczyn – I Turnus Rehabilitacyjny dla Chorych ze szpiczakiem  
mnogim Nałęczów – kwiecień 2018 roku (10 minut)**

Panel dyskusyjny na temat uzasadnienia i korzyści z rehabilitacji  
onkologicznej? Czy to powinno być refundowane przez NFZ?

**PO ZAKOŃCZENIU SPOTKANIA ZAPRASZAMY NA POCZĘSTUNEK**

**GRUPY WSPARCIA** przy pomocy Fundacji Centrum Leczenia Szpiczaka  
będą odbywać się regularnie w każdy ostatni wtorek miesiąca,  
kolejne Spotkanie w dniu 26 czerwca 2018 roku



Zgłoszenia – Artur Jurczyszyn e-mail: [mmjurczy@cyf-kr.edu.pl](mailto:mmjurczy@cyf-kr.edu.pl)

**Obiekt: Termy Pałacowe**

*Pobyt Lecznicy Termy Pałacowe Intensywna Kuracja Uzdrowska*

**Termin: od 16 do 30 września 2018 rok**

**W cenie pakietu:**

- 14 dób - zakwaterowanie w pokojach standard
- wyżywienie całodzienne w restauracji Termy Pałacowe
- 4 zabiegi na dobę zlecone przez lekarza (oprócz niedziel i świąt)
- wizyta lekarska na początku pobytu
- nieograniczony wstęp do kompleksu wodnego Atrium i na basen w Termach Pałacowych



**Cennik:**

**Pokój 1-osobowy: 265zł/osoba/doba –15% = 225, 25 zł/ 1 doba/ 1 osoba**

**Pokój 2-osobowy: 399/doba dla dwóch osób – 15% = 339, 15 zł/ 1 doba**

- *Pobyt odbywa się w obiekcie Termy Pałacowe gdzie nie zapewniamy opieki pielęgniarstwa.*
- *Wizyta lekarska odbywa się w na terenie Parku Zdrojowego w wybranym obiekcie sanatoryjnym.*
- *Zabiegi lecznicze realizowane są w obiektach sanatoryjnych Uzdrowiska Nałęczów lub w Termach Pałacowych.*

# www.szpiczak2018.jordan.pl

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**VII International Conference**  
**„Complex treatment of plasma cell dyscrasia in 2018”**  
Kraków, September 1st 2018 (Saturday) 2.00 PM  
LOCATION: International Cultural Center, Rynek Główny 25

The Honorary Patronage:  
 Marshal of the Malopolska Voivodeship  
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14.15 - 14.25 assoc. prof. **Artur Jurczyszyn**, prof. **Aleksander B. Skotnicki**,  
Jagiellonian University Faculty of Medicine Department of Hematology, Kraków – opening the conference

14.25 - 14.30 prof. **MACIEJ MAŁECKI** MD PhD  
Dean of Faculty of Medicine Jagiellonian University Medical College, Kraków - opening the conference

14.30 - 15.00 prof. **SAGAR LONIAL**  
Emory University, Atlanta, GA, USA  
„Multiple myeloma – the best therapy for newly diagnosed patients in 2018”

15.15 - 15.45 prof. **NOOPUR RAJE**  
Harvard Medical School, Boston, MA, USA  
„Management of bone disease in myeloma: what is the optimal radiographic evaluation and treatment”

16.00 - 16.30 prof. **DAVID H. VESOLE**  
John Theurer Cancer Center, Hackensack University Medical Center, NJ, USA  
„Treatment of relapsed/refractory multiple myeloma: many new therapies”

16.45 - 17.15 prof. **LAURENT GARDERET**  
Hopital Saint Antoine, Service d’hématologie et thérapie cellulaire, Paris, France  
„Role of auto and allo stem cell transplantation in the era of novel drugs in multiple myeloma in 2017”

COFFEE BREAK until 17.45

17.45 - 18.15 prof. **IRIT AVIVI**  
Tel Aviv Medical Center, Tel Aviv, Israel  
„Hematologic malignancies in pregnancy”

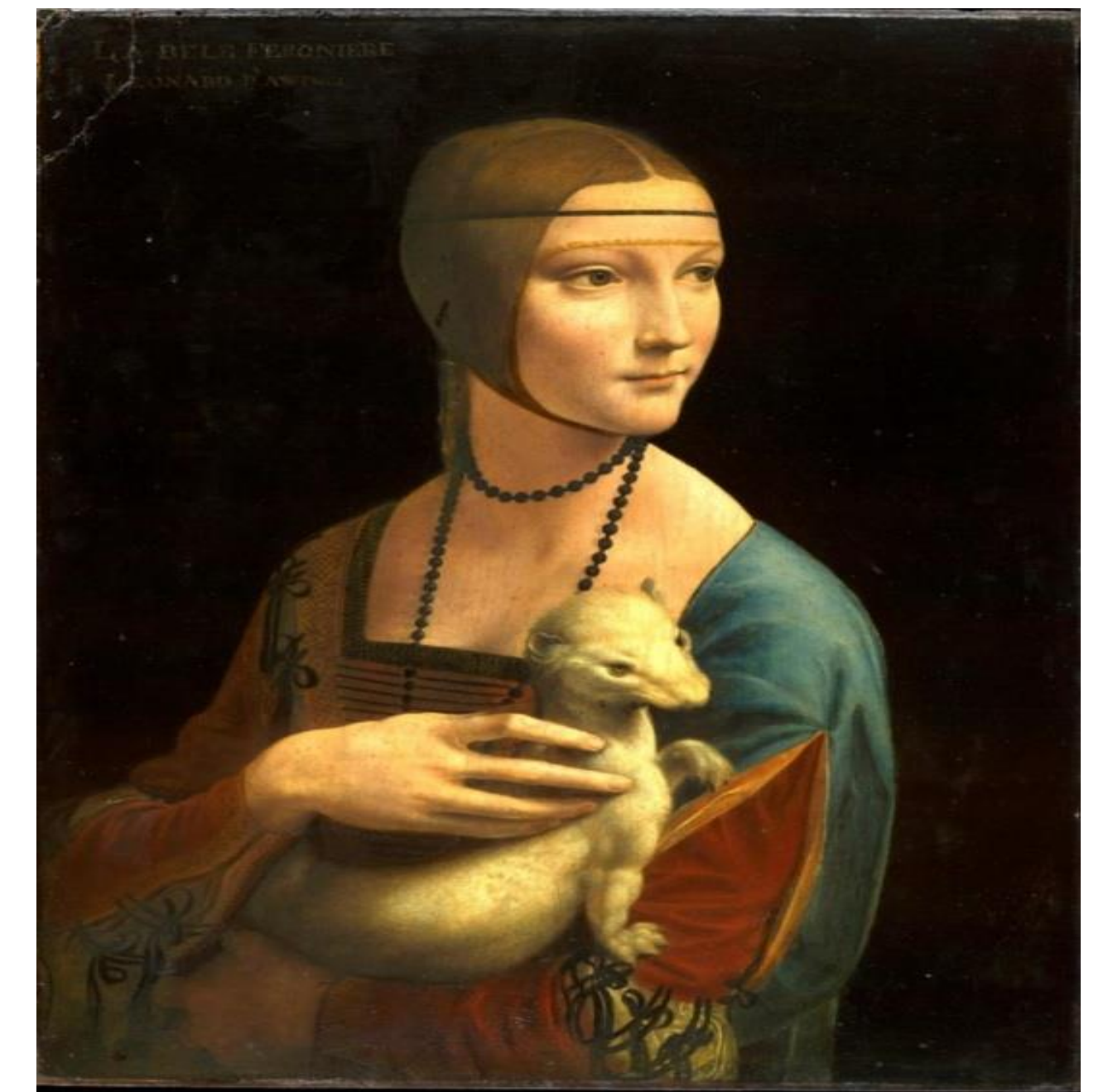
18.30 - 19.00 prof. **SAMIR PAREKH**  
Icahn School of Medicine at Mount Sinai, New York, USA  
„Integrated Genomics approach to Precision Medicine in myeloma”

19.15 - 19.45 prof. **LEO RASCHE**  
UAMS Myeloma Institute, Little Rock, Arkansas, USA  
„Understanding the negative prognostic impact of intraosseous focal lesions in multiple myeloma”

Application at: [fundacja@szpiczak.org](mailto:fundacja@szpiczak.org)

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Lady with Ermine, Kraków,  
Leonardo da Vinci



Salt Mine, Wieliczka

Athens 26-27 OCTOBER 2018

# Educational Workshops



Meletios A. Dimopoulos, MD

Evangelos Terpos, MD

National and Kapodistrian University of Athens, Athens, Greece