

Waldenström's Macroglobulinemia Familial and Secondary Malignancies

**Patient Session
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DISCLOSURE

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Risk of MGUS and Lymphoproliferative Malignancies in First-Degree Relatives of MGUS Patients

MGUS=4458

1° relatives=14,621

	First-Degree Relatives	RR
MGUS	22	2.8
Multiple Myeloma	41	2.9
LP/WM	8	4.0
Chronic Lymphocytic Leukemia	23	2.0
Non-Hodgkin's Lymphoma	44	1.1
Hodgkin Lymphoma (<45 y)	8	1.3
Hodgkin Lymphoma (>45 y)	1	0.2



Risk of MGUS and Lymphoproliferative Malignancies in First-Degree Relatives in IgG/IgA MGUS

N=7490

	First-Degree Relatives	RR
MGUS	15	4.0
Multiple Myeloma	22	2.9
LP/WM	5	20.0
Chronic Lymphocytic Leukemia	11	1.5

Risk of MGUS and Lymphoproliferative Malignancies in First-Degree Relatives in IgM MGUS

N=1696

	N	RR
Multiple Myeloma	2	1.9
LPL/WM	1	3.5
CLL	4	5.0

Lymphoplasmacytic Lymphoma(LPL)/ Waldenström's Macroglobulinemia (WM)

N=2144

First-Degree Relatives

Types of first-degree relatives (parent, sibling, offspring)

Age at diagnosis > 70, < 70

Male or Female

The risks are not different in all categories

Relative Risk of LPL/WM in First-Degree Relatives

N=2144

(WM=1539, LPL=605)

	Patients (N)	RR
LPL/WM	10	20.0
Non-Hodgkin's Lymphoma	43	3.0
Chronic Lymphocytic Leukemia	16	3.4
Hodgkin Lymphoma	4	0.8
Multiple Myeloma	11	1.6
MGUS	5	5.0

Relative Risk of Myeloid Malignancies in First-Degree Relatives of LPL/WM Patients

	Relatives of LPL/WM	RR
AML/MDS	9	1.7
Chronic Myeloproliferative	6	0.6
Chronic Myeloid Leukemia	3	1.0
Solid Tumors	581	1.08

Waldenström's Macroglobulinemia in Second Malignancies

N=1618
1973-2008

	SIR*
AML	5.3
NHL	4.9
Myeloma	4.4
Colon	2.2
Uterus	2.2
Lung	1.6
All lymphoproliferative	3.8
All solid tumors	1.4

*SIR: Standardized Incidence Ratio



Ojha RP et al., Annals Oncol 23:542, 2012

Waldenström's Macroglobulinemia

N=257

First-Degree Relatives	RR
WM	5.1
Non-Hodgkin's Lymphoma	3.5
Multiple Myeloma	3.1
Chronic Lymphocytic Leukemia	2.7
MGUS	1.9
ALL	1.2
Hodgkin's disease	1.2
Total	18.7

Waldenström's Macroglobulinemia Second Malignancies

SEER 1992-2011

	MP-SIR*
All lymphomas	4.4
Myeloma	4.7
Acute leukemia	3.2
All hematologic	4.2

*MP-SIR Multiple Primary Standardized Incidence Ratio
of normal population

Castillo JJ et al., Cancer 121:2230, 2015

Waldenström's Macroglobulinemia Second Malignancies

SEER 1992-2011

	MP-SIR*
Thyroid	2.7
Melanoma	1.9
Lung	1.5
Breast	1.04
Colorectal	0.92
All solid tumors	1.2

*MP-SIR Multiple Primary Standardized Incidence Ratio
of normal population

Waldenström's Macroglobulinemia in Non-Hematologic Malignancies

1999-2016

	A/E	RR
Breast	115/103	1.1
Colorectal	72/71	1.0
Lung	83/95	.86
Ovarian	15/20	.75
Prostate	79/59	1.4

Waldenström's Macroglobulinemia Second Malignancies

N=230

	N	SIR*
DLBCL	6	8.6
MDS/AML	4	9.5
Brain	2	7.6
Thyroid	1	4.8
Urinary Tract	4	2.1
Breast	3	1.5
Lung	4	1.4
Prostate	4	1.3
GI Tract	6	1.1
All Cancers	35	1.7

Morra E et al., Clin Lymph Myeloma & Leukemia 13:700, 2013

*Standardized Incidence Ratio

Waldenström's Macroglobulinemia Second Malignancies

**Fludarabine + Rituximab Therapy
N=43**

Follow-up 40.3 mos

	N
Lymphoma	3
MDS/AML	3

Treon S et al., Blood 113:3673, 2009

Waldenström's Macroglobulinemia Second Malignancies with Fludarabine Therapy

N=176

MDS/AML	19 (10.8%)
OS	11 months

Carney DA, Leukemia 24:2056, 2010

Waldenström's Macroglobulinemia Second Malignancies

	N
WM	339
Marginal Zone	37
Lymphoplasmacytic lymphoma (LPL)	38

Leblond V et al., JCO 31:301, 2013

Waldenström's Macroglobulinemia Second Malignancies

N=339

	6 yr
Chlorambucil	20.6%
Fludarabine	3.7%

Leblond V et al., JCO 31:301, 2013

Waldenström's Macroglobulinemia

N=2185

Risk of Death

Family History	N.	HR
Any LP	93	1.34
Multiple Myeloma	13	1.47
NHL	44	1.43
CLL	17	1.43
LPL/WM	16	1.28

Waldenström's Macroglobulinemia

No. of Patients per Family	No. of Families
2	3
3	1
4	5
5	1

McMaster ML et al., Am. J. Hum. Genet. 79:695, 2006

Waldenström's Macroglobulinemia

Second Malignancies

Incidence of WM:

0.5 persons/100,000

Double risk:

1.0 persons/100,000

Quadruple risk:

2.0 person/100,000

