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## **Solitary plasmacytoma: Lenalidomide-Dexamethasone combined with radiation therapy improves progression-free survival and multiple myeloma-free survival**

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### **Short title**

Combined radiation for solitary plasmacytoma

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## **ABSTRACT**

**Purpose:** To evaluate the results of the concurrent use of lenalidomide-dexamethasone with intensity-modulated radiation therapy (IMRT) for solitary plasmacytoma in terms of toxicity and outcome

**Materials & Methods:** Forty-six patients were treated for histologically proven SP between June 2007 and June 2018 in our Department (XXX). All patients received IMRT. The median total dose was 40 Gy (range, 40-46). Prescription of concurrent lenalidomide-dexamethasone with radiotherapy was left discretion of the referring hematologist-oncologist and started the first day of radiotherapy for four cycles.

**Results:** Twenty-seven solitary plasmacytoma were treated with IMRT alone and 19 with lenalidomide-dexamethasone in association with IMRT. At 5 years, the local control, multiple myeloma-free survival (MMFS) and progression-free survival (PFS) rates were 96.3%, 85.4%, and 60%. MMFS and PFS were significantly higher in the IMRT plus lenalidomide-dexamethasone group compared to IMRT alone group (100% vs 77.1%,  $p=0.02$  and 81.7% vs 48.4%,  $p=0.047$ , respectively). No major toxicity was found in either group.

**Conclusion:** Lenalidomide-dexamethasone in association with IMRT in the treatment of solitary plasmacytoma is safe and improves MMFS and PFS. Further prospective and comparative studies are needed to confirm these results.

## INTRODUCTION

Solitary plasmacytoma (SP) is a rare tumor characterized by localized clonal plasma cell infiltration without clonal bone marrow plasma cells and with no of end-organ damage (1).

The infiltration may arise in the bone (solitary bone plasmacytoma (SBP)) or, more rarely (2–4), extraosseous sites (extramedullary plasmacytoma (EMP)).

SP are radiosensitive tumors and radiation therapy (RT) achieves good long-term local control (5-years: 85% to 95% (3,5–9); 10-years: 86-87% (6,8). Definitive RT is therefore now the standard treatment for SP and the International Lymphoma Radiation Oncology Group has recently published guidelines on the issue (10).

The most dreaded event is progression to multiple myeloma (MM). Many authors have therefore proposed an association of systemic therapy and RT to treat occult disease outside the irradiation field (4,11–14) and numerous studies have been conducted (3,11,13,15–17).

The idea of associating new-targeted and well tolerated treatments with IMRT is coming after observation of patients treated with this combined treatment for myeloma with interesting results (15).

The efficacy data for lenalidomide (Revlimid®), in association with dexamethasone for first-line treatment of multiple myeloma in transplant-ineligible patients, are based on the phase III FIRST study (18). The FIRST study is an open-label, randomized, three-arm study that compared the efficacy of lenalidomide-dexamethasone in two treatment arms (either until disease progression (Rd group) or for up to 18 cycles (Rd18 group) versus melphalan-prednisone-thalidomide (MPT group; 12 cycles).

After median follow-up of 3 years, median PFS was 25.5 months in the Rd group compared to 21.2 months in the MPT group (HR=0.72; 95%CI [0.61- 0.85]; p<0.01) and 20.5 months in the Rd18 group (18).

Lenalidomide-dexamethasone in association with intensity modulated radiation therapy (IMRT) in the treatment of SP could therefore be an interesting approach to reducing MM progression. The objective of this study is to determine the impact on survival and safety of a modern combination of lenalidomide-dexamethasone and IMRT with a longer follow-up in larger series of SP.

## **MATERIALS AND METHODS**

### *Patients*

All patients treated with concomitant lenalidomide-dexamethasone and IMRT (IMRT-LenDex group) for histologically proven SP at the XXX were included in this retrospective study. Patients treated for SP with chemotherapy or proteasome inhibitors or thalidomide during radiotherapy were excluded, as well as patients who received consolidation adjuvant treatment after radiotherapy. Patients who underwent decompressive laminectomy, or spine stabilization and who were subsequently treated by IMRT were also included while patients with surgical resection were excluded. The first patient was treated in June 2007 and inclusion in the study was stopped in June 2018. The inclusion criteria and inclusion period for this study differed slightly from our last published study, however we included the 13 patients in the IMRT alone group as well as the 7 patients in the IMRT-LenDex group from the previous study (flow chart: Figure 1).

SP was confirmed histologically with biopsy and clinical work-up to confirm the absence of any features for MM, according to guidelines (1,19). In particular, bone marrow biopsy was systematically performed to rule out MM at diagnosis, but also in the event of suspected myeloma progression or relapse of a new SP.

### *Data collection chapter*

The prospective registration of these patients treated for SP in our hospital with highly effective radiation techniques (TomoTherapy®) was accepted by the Hematological Malignancies Group in the Department of Radiation Oncology and a special case report form (CRF) was developed for data collection after discussion in the Institutional Hematological Malignancies Study Group. This procedure was introduced in 2007 when the first TomoTherapy® machine arrived in our Department. The radiation oncologist completed the CRF for every new patient.

*Treatments and follow-up*

IMRT delivered 40 Gray (Gy) for SBP and 46 Gy for EMP in 20-23 fractions by helical TomoTherapy®. The gross tumor volume (GTV) was contoured (Eclipse 3D, Varian Medical Systems Inc.) using 18-fluoro-deoxyglucose positron emission tomography-computed tomography (PET-CT) and/or magnetic resonance imaging fused with planning CT scan. The clinical target volume (CTV) was generated by adding a 2-3 cm margin in all directions from the GTV (with respect to anatomical barriers) according to guidelines from the International Lymphoma Radiation Oncology Group (10). An additional 0.5-1 cm margin was added to the CTV to define the planning target volume (PTV) and dose calculation was performed using the helical TomoTherapy® treatment planning system (Tomo-Therapy HI-ART, TomoTherapy Inc., Madison, USA). The treatment planning objective was to ensure 95% coverage of the PTV volume by 95% of the prescribed dose while respecting dose constraints on organs at risk.

The decision to associate lenalidomide and IMRT was left to the discretion of each referring hematologist in collaboration with the radiation oncologist. In practice, some referring hematologists systematically accepted concurrent lenalidomide and IMRT while others refused. The decision was not based on population or tumor criteria.

Lenalidomide was administered orally at a dose of 25mg/day for 21 days, followed by an 8-day break before the next cycle, with a total of 4 cycles. The first dose of lenalidomide was administered on the first day of radiotherapy. Dexamethasone (40mg/week) was routinely added to lenalidomide, but was sometimes started before radiotherapy.

A physical examination was performed at Week 6 and physical, laboratory and radiological (PET-CT) examinations were performed at Month 4, then every 6 months alternately by the hematologist and the radiation oncologist for 2 years and then annually. Toxicities were reported according to CTCAE v5.0.

### *Statistics*

Multiple myeloma-free survival (MMFS) was defined as the time from end of IMRT until progression to MM. Patients without progression to MM were censored. Plasmacytoma relapse-free survival (PRFS) was defined as the time from the end of IMRT until relapse of plasmacytoma (excluding local relapse, i.e. other plasmacytoma sites without evidence to progression to MM). Patients without plasmacytoma relapse were censored. Local relapse-free survival (LRFS) was defined as the time from the end of IMRT until local progression of irradiated plasmacytoma, confirmed by PET-CT.

Progression-free survival (PFS) was defined as the time from the end of IMRT until the time of plasmacytoma progression or progression to MM or death. Survival curves were estimated using the Kaplan–Meier method from the end of IMRT and were compared between groups using log-rank tests. Cox regression analysis was used to identify prognostic factors. All statistical analyses were performed with R software (version 3.22; <https://cran.r-project.org/>). The limit of significance was set at  $p < 0.05$ .

## RESULTS

Forty-six patients treated for SP were included with median follow up of 5.3 years. The median age of the patients was 57.3 years (range 28-75).

Forty (87.0%) of the 46 irradiated SP were SBP and 6 were EMP (13.0%).

The detail of localizations is presented in appendix - Table S1. The mean diameter of SBP was 64.8 mm (range 15-140) and the mean diameter of EMP was 35.8 mm (range 15-53).

A monoclonal immunoglobulin peak was detected in 26 patients (56.5%), mainly IgG; and Bence-Jones proteinuria was presented in 9 patients (19.6%).

The median CTV volume was 126.8 cm<sup>3</sup>, and all patients received the prescribed dose, except for one patient who stopped radiation therapy at 26 Gy due to a psychiatric disorder.

Twenty-seven SP were treated with IMRT alone (58.7%) and 19 were treated with lenalidomide-dexamethasone in association with IMRT (41.3%).

Patient characteristics, laboratory parameters and tumor description are presented in Table 1.

No significant differences were observed between patients treated with IMRT alone (IMRT alone group) and patients treated with lenalidomide-dexamethasone in association with IMRT (IMRT-LenDex group) (Table 1). The median CTV volume was of 116.4 cm<sup>3</sup> in the IMRT alone group and 169.3 cm<sup>3</sup> in the IMRT-LenDex group (p=0.20).

### *Survival outcomes*

Five-year overall survival rate, local control, multiple myeloma- and progression-free survival rates were 94.8%, 96.3%, 85.4%, and 60.0% respectively.

MMFS (100% vs 77.1%, p=0.02) and PFS (81.7% vs 48.4%, p=0.047) were significantly higher in the IMRT-LenDex group compared to IMRT alone group. (Figures 2A and 2B).

No progression to MM occurred in the IMRT–LenDex group. Only two local relapses were diagnosed in patients who had IMRT alone and one in the IMRT–LenDex group (p=0.84).

On univariate analysis, age > 60 years (trend with  $p=0.05$ ) and IMRT alone ( $p<0.03$ ) were risk factors for poor MMFS. IMRT alone versus lenalidomide-dexamethasone with IMRT was also in poor prognosis for PFS (HR 3.30; 95CI% [1.01-11.48],  $p<0.05$ ). The presence of EMP versus SBP was predictive of a better prognosis in terms of overall survival (HR 0.08; 95CI% [0.01-0.87],  $p=0.04$ ) (Table 2).

No significant differences were observed for overall survival, LRFS and PRFS between the two groups (Appendix Figures S1 to S3).

### *Toxicity*

Ten patients (21.7%) presented grade-1 radiation induced dermatitis without significant difference between the 2 groups. Hematological toxicity, i.e. neutropenia and thrombocytopenia, was higher in the IMRT-LenDex group, but without significant difference.

A pain flair after IMRT for SP treatment (defined by a transient increase in pain or change in analgesic level during radiotherapy) was found in 10 patients (21.7%) with no significant difference between the 2 groups and despite dexamethasone in the IMRT-LenDex group.

Grade 1-2 diarrhea was observed in 23.1% of patients ( $n=3/13$ ) with SP in the pelvis, sacrum, or lumbar spine who received radiation to the digestives tract. One patient in the IMRT-LenDex group had flu-like syndrome and one had a urinary tract infection without severity.

One patient stopped lenalidomide due to rash but outside the irradiation fields, and another patient stopped lenalidomide due to a superficial hematoma during anticoagulant therapy.

No grade 4 or 5 toxicity was reported. The toxicity is presented in Table 3.

## DISCUSSION

In this study, the lenalidomide-dexamethasone in association with IMRT in the treatment of SP improved PFS and MMFS with acceptable toxicity of combined therapy.

The concept of associating systemic therapy with RT to treat SP is not a new approach. It is based on the assumption that progression to MM can occur as a result of an occult disease situated outside the irradiation field.

To investigate this hypothesis, Hill et al. used multiparameter flow cytometry to evaluate the presence of occult disease in bone marrow samples, in patients with SBP, defined as a discrete population of plasma cells with phenotypic aberrations and representing > 30% of the population. They showed that 68% of a series of 50 patients had occult disease, which was a predictive factor for disease progression (72% of patients with occult disease versus 12.5% of those without occult disease with follow-up of 3.7 years) (12).

Several studies with a low level of evidence have evaluated the benefit of systemic treatments in association with RT for the treatment of SP (Table 4).

A prospective study by Aviles, in 1996, demonstrated that melphalan improved overall survival ( $p < 0.01$ ) and MMFS ( $p < 0.01$ ), with median follow-up of 9.8 years (11).

In a multicenter study by Ozsahin et al. in 2006 on the patterns and outcomes of failure in SP in a series of 258 patients, 13% of patients received chemotherapy (melphalan and prednisone or vincristine, doxorubicin and dexamethasone or other combinations) and RT.

At 10 years there were no significant differences (univariate analyses) between the 2 groups on local control ( $p = 0.24$ ), MMFS ( $p = 0.74$ ) or DFS ( $p = 0.80$ ), but the radiation doses were different with a significant impact on local control (3).

In a Greek study with 97 patients where about one-third of the patients had RT alone and one-third had a RT in association with systemic treatment (the last third had other treatment modalities), there were no significant differences on MMFS or OS (13).

In an abstract published in 2016 in the journal *Blood*, the 5-year PFS rate in the RT group was 27.5%, versus 53.6% in the RT plus systemic treatment group ( $p=0.31$ ). In this multicenter study on 65 patients, 20 patients received adjuvant treatment based on melphalan or bortezomid or thalidomide and corticosteroids and 32 patients received RT alone. As in our study, no impact was observed on overall survival (17).

Overall, the studies did not show any significant differences however there was a trend towards longer PFS in the RT plus systemic treatment groups. The diversity of treatment modalities, i.e. low dose of radiation, chemotherapy and/or PI and/or IMiD drug-based regimens, excision surgery, precise timing with RT not known could have influenced the results (3,11,13,15,17).

This study, based on a larger sample of patients with longer median follow-up, confirms our previous data on PFS (15). In our previous study based on 28 patients with median follow-up of 53 months, new agents in association with RT improved the PFS, at 80% vs 50.3% with RT alone ( $p < 0.032$ ). This study provides new and significant results concerning MMFS demonstrating the benefit of adding Len-Dex during IMRT.

Traditionally and in most studies from the literature, the 5-year rate of progression to MM ranges between 42% and 54% (3,9,11,13,20,21). The progression rate of 14.6% observed in our study may therefore appear to be unusually low. However, we have performed bone marrow biopsy in the event of suspected progression to multiple myeloma or recurrence of multiple plasmacytoma. No progression to MM was observed in the IMRT-LenDex group and the multiple myeloma progression rates was 22.9% in the IMRT alone group.

In addition, we included 13% of EMP which is a known prognostic factor for better prognosis (5).

In 2015, an Italian study reported an MM progression rate of 16.5% at 5 years and 5-year PFS of 66.3%, which is close to our findings (22).

Concerning the overall survival and local relapse rate, our results are consistent with those of the literature and we also found prognostic factors (age > 60 years and SPB) already described in the literature (13,22,23).

This study also confirms that the use of IMRT in the treatment of SP provides excellent local control with no grade 2 or higher acute radiation dermatitis (16,24,25). In the recently published guidelines from ILROG, IMRT is recommended as a modern technique that reduces the doses to organs at risk and delivers homogeneous coverage of complex volumes (10). The improved coverage could explain the excellent results in terms of local control.

Our study is not without limitations including its retrospective nature, the limited number of patients, especially after exclusion of patients with other systemic treatment, as well as patients with multiple plasmacytoma. There is also possible selection bias related to the treatment decision of different medical oncologists and hematologists, however it is limited because one of the teams proposed Len-Dex and IMRT to all patients treated during this period and based on the results of this study they continue to propose it as standard. Other teams preferred the classic approach using IMRT alone. The two groups were nevertheless equally balanced. Because of the small numbers of patients and small number of events, our results must be interpreted with caution. However, this study provides new and significant results in favor of concomitant irradiation in a rare disease and using recent treatments, both drug-based (Len-Dex) and radiotherapy (by IMRT).

We are aware of one ongoing phase III study (IDRIS Trial, NCT02544308) of patients with high-risk SBP addressing adjuvant lenalidomide-dexamethasone after (not concurrent with) radiation therapy to prevent the occurrence of multiple myeloma.

In conclusion, our preliminary data suggests that the association of lenalidomide-dexamethasone with IMRT in the treatment of solitary plasmacytoma seems safe and

improves multiple myeloma- and progression-free survival but further prospective studies must be conducted.

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**FIGURES with legends**

Figure 1: Flow chart

SBP: solitary bone plasmacytoma; RT: radiation therapy; IMRT: intensity-modulated radiation therapy; 3D: 3-dimension; n=number

Figure 2: Survival outcomes

A: Multiple Myeloma-Free Survival

B: Progression-Free Survival

IMRT: intensity-modulated radiation therapy

IMRT + LenDex: intensity-modulated radiation therapy plus lenalidomide-dexamethasone

Table 1: Characteristics of population

SBP: solitary bone plasmacytoma; EMP: extramedullary plasmacytoma; IMRT: intensity-modulated radiation therapy; Ig: immunoglobulin; n=number; CTV: clinical target volume

Table 2: Univariate analysis on survival

SBP: solitary bone plasmacytoma; EMP: extramedullary plasmacytoma; IMRT: intensity-modulated radiation therapy; CTV: clinical target volume; LC: local control; MMFS: multiple-myeloma free survival; PFS: progression free survival; OS: overall survival; HR: hazard ratio  
-: in the absence of any event in one of the two groups, according to Cox's formula it is not possible to calculate a hazard ratio

Table 3: Toxicities

IMRT: intensity-modulated radiation therapy

IMRT + LenDex: intensity-modulated radiation therapy plus lenalidomide-dexamethasone

Table 4: Studies from the literature with a comparison survival outcome between RT alone group and RT combined treatment group

FU: follow-up; nc: not communicated; SBP: solitary bone plasmacytoma; EMP: extramedullary plasmacytoma; RT: radiation therapy; MM: multiple myeloma; PFS: progression-free survival; OS: overall survival; DFS: disease-free survival; HR: hazard ratio; IMRT: intensity-modulated radiation therapy; 3D: 3-dimension; Mel: melphalan; Pred: prednisone; VD: vincristine-dexamethasone; bort: bortezomib; cort: corticosteroid; len: lenalidomide; IMiD: immunomodulatory drug; thal: thalidomide; dex: dexamethasone; y: years

**SUPPLEMENTARY MATERIAL**

Figure S1: Overall survival

IMRT: intensity-modulated radiation therapy

IMRT + LenDex: intensity-modulated radiation therapy plus lenalidomide-dexamethasone

#### Figure S2: Local Relapse-Free Survival

IMRT: intensity-modulated radiation therapy

IMRT + LenDex: intensity-modulated radiation therapy plus lenalidomide-dexamethasone

#### Figure S3: Plasmacytoma Relapse-Free Survival

IMRT: intensity-modulated radiation therapy

IMRT + LenDex: intensity-modulated radiation therapy plus lenalidomide-dexamethasone

#### Table S1: Localization of SP

IMRT: intensity-modulated radiation therapy; LenDex: lenalidomide-dexamethasone; SBP: solitary bone plasmacytoma; EMP: extramedullary plasmacytoma

Figure 1: Flow chart

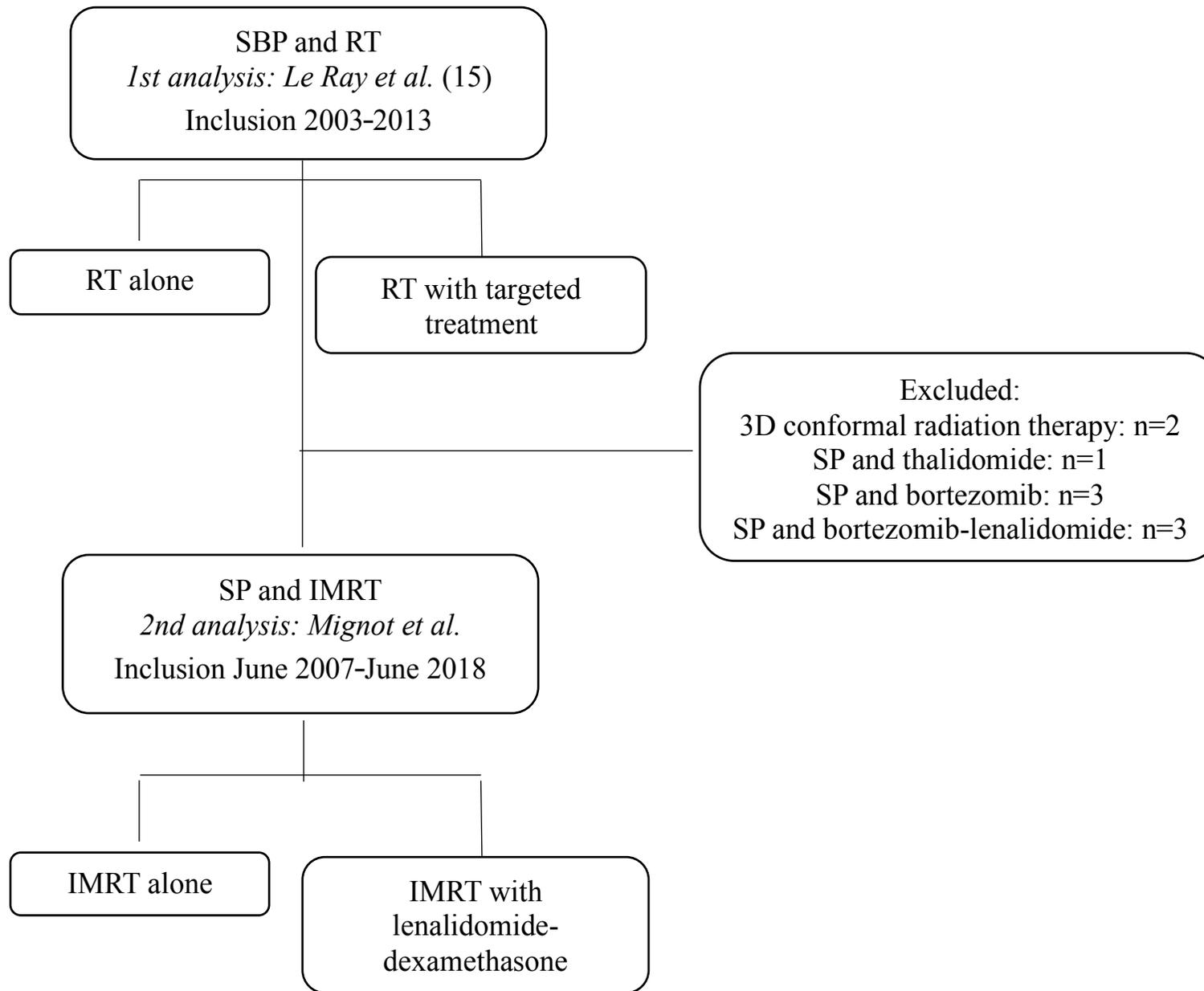
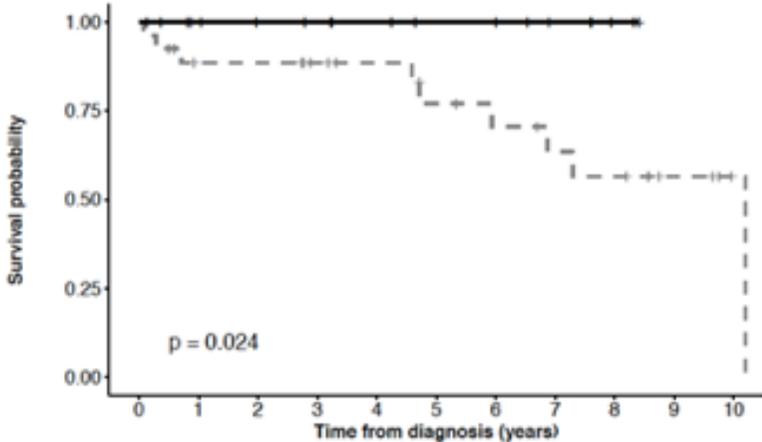


Figure 2: Survival outcomes

A: Multiple Myeloma-Free Survival (MMFS)

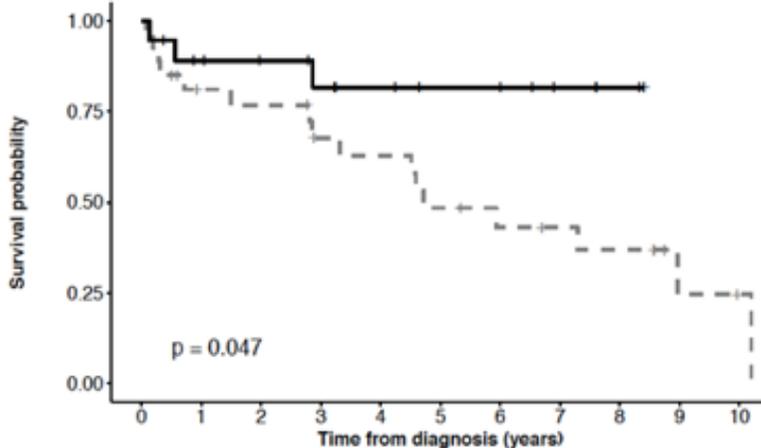


Number at risk

IMRT	27	21	21	18	16	13	11	9	8	4	1
IMRT + LenDex	19	15	13	12	10	8	8	5	2	0	0
	0	1	2	3	4	5	6	7	8	9	10

→ IMRT ⇨ IMRT + LenDex

B: Progression-Free Survival (PFS)



Number at risk

IMRT	27	19	18	14	13	10	8	7	6	2	1
IMRT + LenDex	19	15	13	11	9	7	7	4	2	0	0
	0	1	2	3	4	5	6	7	8	9	10

→ IMRT ⇨ IMRT + LenDex

Table 1: Characteristics of population

	<b>Global</b>	<b>IMRT alone group</b>	<b>IMRT-LenDex group</b>	<b>P value</b>
<b>N</b>	46	27	19	
<b>Age median (range)</b>	57.3 (28-76)	58.8 (30-76)	55.7 (28-74)	0.76
<b>Sexe</b>				1.0
Female (%)	11 (23.9)	6 (22.2)	5 (26.3)	
Male (%)	35 (76.1)	21 (77.8)	14 (73.7)	
<b>SBP</b>	40 (87.0)	23 (85.2)	17 (89.5)	1.0
<b>EMP</b>	6 (13.0)	4 (14.8)	2 (10.5)	
<b>Tumor size median mm (range)</b>	50 (15-140)	53 (15-140)	50 (15-90)	0.71
<b>SUV max median (range)</b>	8.7 (0-26.9)	10.1 (0-26.9)	5.1 (0-19.2)	0.15
<b>Ig-peak: positive n (%)</b>	25 (54.3)	17 (63.0)	8 (42.1)	0.40
IgG	22 (47.8)	15 (55.6)	7 (36.8)	
IgA	3 (6.5)	1 (3.7)	2 (10.5)	
IgM	1 (2.3)	1 (3.7)	0	
<b>Bence-Jones proteinuria (%)</b>	9 (19.6)	6 (22.2)	3 (15.8)	0.86
<b>Surgery of consolidation before RT (%)</b>	8 (17.4)	5 (18.5)	3 (15.8)	0.56
<b>Dose RT median (range)</b>	40 (26-46)	40 (40-46)	40 (26-46)	
<b>CTV volume (range) cm<sup>3</sup></b>	126.8 (5.0-784)	116.4 (5.0-567.4)	169.3 (32.9-784)	0.20

Table 2: Univariate analysis on survival

	LC		MMFS		PFS		OS	
	HR 95%CI	p	HR 95%CI	p	HR 95%CI	p	HR 95%CI	p
<b>Age &gt;60y</b> (vs ≤60y)	1.02 0.09-12.28	0.99	2.05 0.51-8.22	0.05	1.91 0.75-4.87	0.17	-	NS
<b>Sexe</b> (Male vs Female)	-	NS	0.25 0.06-1.05	0.06	0.98 0.32-3.00	0.97	0.65 0.06-7.21	0.73
<b>EMP</b> (vs SPB)	-	NS	-	NS	1.23 0.28-5.40	0.78	0.08 0.01-0.87	0.04
<b>CTV &gt;130cm<sup>3</sup></b> (vs ≤130cm <sup>3</sup> )	1.00 0.99-1.00	0.48	1.00 0.99-1.00	0.19	0.99 0.99-1.00	0.59	1.00 0.99-1.00	0.32
<b>IMRT alone</b> (vs IMRT-LenDex group)	1.28 0.11-14.10	0.80	-	<0.03	3.30 1.01-11.48	<0.05	1.19 0.11-13.24	0.88

Table 3: Toxicities

	Global	IMRT alone group	IMRT-LenDex group	P value
<i>percent of patients</i>				
<b>Acute radiation dermatitis</b>				
0	78.3	77.8	78.9	0.82
1-2	21.7	22.2	21.1	
≥ 3	0	-	-	
<b>Thrombocytopenia</b>				0.10
0	95.6	100	89.5	
1-2	4.3	0	10.5	
≥ 3	0	-	-	
<b>Neutropenia</b>				0.18
0	91.3	96.3	84.2	
1-2	6.5	3.7	10.5	
≥ 3	2.2	0	5.3	
<b>Diarrhea</b>				0.72
0	91.3	92.6	78.9	
1-2	8.7	7.4	21.1	
≥ 3	0	-	-	
<b>Pain flare</b>				0.79
No	78.3	81.5	73.7	
Yes	21.7	18.5	26.3	
<b>Others</b>				NC
Flu-like syndrom	2.2	0	5.3	
Urinary sepsis	2.2	0	5.3	
Dysphagia gr1	4.3	3.7	5.3	
Mucositis gr1	4.3	3.7	5.3	
Rash	2.2	0	5.3	
Hematoma	2.2	0	5.3	

Table 4: Studies from the literature with a comparison survival outcome between RT alone group and RT combined treatment group

	<i>Aviles et al. (11) 1996</i>	<i>Ozsahin et al. (3) 2006</i>	<i>Katodritou et al. (13) 2014</i>	<i>Mheidly et al. (17) 2016</i>	<i>Le ray et al. (15) 2018</i>	<i>Mignot et al. 2019</i>
Comparison between RT alone group and RT combined treatment* group						
<b>Patients (n)</b>	53	258	97	52	28	46
<b>Median FU (y)</b>	9.8	4.7	5.0	4.6	4.3	5.3
<b>SBP (%)</b>	100	80	67	100	100	87
<b>EMP (%)</b>	-	20	33	-	-	13
<b>Risk factors predicting poor survival outcomes</b>	nc	Age > 60, SBP, tumor size	Age > 60, immunoparesis	nc	nc	Age > 60, SBP
<b>Systemic treatment*</b>	Mel-Pred n=25 (47%)	Mel-Pred or VD-dex or others n=33 (13%)	Chemo or Bort-cort or IMiD-cort n=46 (47%)	Mel-cort Len-cort or Bort-cort or Thal-cort n=20 (38%)	Len-Dex or Bort-Dex or Bort-Len-Dex or Thal n=13 (46%)	Len-Dex n=19 (41%)
<b>Therapy regimen</b>	Adjuvant	nc	Adjuvant	Adjuvant	Concomitant	Concomitant
<b>Dose RT (Gy)</b>	40-50	<30-≥50 (BED)	nc	nc	40	40-46
<b>Modality of radiation</b>	nc	nc	nc	nc	3D and IMRT	IMRT
<b>Significant results on survival (p&lt;0.05)</b>	Better OS and DFS (in RT combined group)	No impact on LC, OS, DFS and MMFS	No impact on OS and MMFS	No impact on PFS, PFS and MMFS	Better PFS (in RT combined group)	Better PFS and MMFS (in RT combined group)
<b>PFS 5 y (%)</b>	nc	10 y - DFS 17 in RT combined group 35 in RT alone group	58 (all cohort)	53.6 in RT combined group 27.5 in RT alone group	80 in RT combined group 50.3 in RT alone group	60 (all cohort) 81.7 in RT combined group 48.4 in RT alone group
<b>OS 5 y (%)</b>	nc	74 (all cohort)	84 (all cohort)	97 in RT combined group 94 in RT alone group	4 y - 95 (all cohort)	94.8 (all cohort)
<b>Progression to MM 5 y (%)</b>	nc	45 (all cohort) 10 y 74 in RT combined group 64 in RT alone group	30 (all cohort)	-	7.7 in RT combined group 33.3 in RT alone group	14.6 (all cohort) 0 in RT combined group 22.9 s in RT alone group