Secondary immunodeficiency in multiple myeloma

SECONDARY
IMMUNE
DEFICIENCY

Immunodeficiency in Multiple Myeloma is due to the underlying disease and its treatment

SECONDARY IMMUNE DEFICIENCY

- Dysfunctional replication of plasma cells
  - Production of large quantities of dysfunctional antibodies (M-proteins)
  - Accelerated catabolism and reduced synthesis of normal immunoglobulins causing a nonparaprotein hypogammaglobulinaemia
- Iatrogenic causes: chemotherapy-induced granulocytopaenia, high-dose corticosteroids…
- Impaired quantity and function of humoral immunity and cellular immunity (abnormalities of B cell, T cell, dendritic cell (DC) and natural killer (NK) cell)
- Myeloma cells increase activity of immunosuppressive cells (regulatory T cells and myeloid-derived suppressor cells (MDSCs)
- Myeloma cells inhibit cytotoxicity of cytotoxic T-lymphocytes (CTLs) and natural killer (NK) cells
- Myeloma cells produce cytokines causing profound dysfunction of various immune cells (i.e., transforming growth factor (TGF)-β, interleukin (IL)-10, IL-6)

Pratt G, et al. Br J Haematol. 2007;138:563–79, Kyrtsonis, M.C. et al., Med Oncol. 1999; 16:73-7, Tamura H. Int J Hematol. 2018;107:278–85., Li L. and Wang, L., J Cancer 2019; 10:1675-84.

Focus on hypogammaglobulinaemia: disease related detailed mechanism in Multiple Myeloma

SECONDARY IMMUNE DEFICIENCY

Soluble immunosuppressive factors secreted by macrophages

- Secretion of plasmacytoma-induced-macrophage substance (PIMS) inhibits B cell proliferation and Ig production
- PIMS production is induced by PC factor secreted by MM cells

Decreased number and function of B cells

- Abnormal B cell maturation due to increased CD5 + B cells that are immunosuppressive
- Suppression of B cell progenitors that may be attributed to attrition of the normal plasma cell (normal plasma cell precursors (CD19+38 +) in the blood as well as normal marrow B cell progenitors, (CD19+ expressing CD5, CD10, CD34, CD38, $CD45^{low}$ and Syndecam-1) are decreased in patients with active disease)
- Increased apoptosis of B cells through an interaction between MM and stroma cells

Immunosuppressive cytokines

- Low IL-4 lead to decreased response of normal B cells
- Suppression of normal B cells by TGF- beta1
- Induction of cell growth arrest by increased E2F transcription factor expression indirectly induced by TGF-beta1

Role of T cells

- Inadequate cytokine production affecting proliferation and differentiation of B cells

Increased catabolism of IgG

- 2-fold increase in the rate of catabolism of both normal and clonal IgG
- The catabolic rate of other Ig classes is not affected

Ig: immunoglobulin, MM: multiple myeloma, IL: interleukin; TGF: transforming growth factor.

Kyrtsonis, M.C. et al., Med Oncol. 1999; 16:73-7.

Iatrogenic causes of SID in Multiple Myeloma

Class of therapy	Immune dysfunction	Infections
Corticosteroids	Cellular immunity[2] Hypogammaglobulinaemia - decreased naïve and transitional B cells, with no effect on memory B cells[2]	Increased incidence of infections[2]
Alkylating agents: e.g. bendamustine	Hypogammaglobulinaemia[2]	Increased incidence of infections[2]
Immunomodulatory drugs (IMIDs): e.g. lenalidomide	Mechanisms unclear[3]	Incidence of high-grade infections increased two-fold with lenalidomide[3]
Proteasome inhibitors (PIs): e.g. bortezomib	Decreased IgG, IgA, and IgM (but not hypogammaglobulinaemia)[2]	Increased incidence of HZ infections and VZV reactivation[2,4]
Anti-CD38 antibody e.g. daratumumab	Risk of neutropaenia[4], with no effect on B cells[2]	Increased incidence of infections (including VZV)[2,4]
Anti-SLAMF7/CD319 antibody e.g. elotuzumab	Lymphopaenia[4]	Lymphopaenia and increase the risk of infection (particularly due to VZV)[4]

Other MM treatments/modes of treatment delivery can also increase the risk of infections:

- HSCT (neutropaenia, gastrointestinal mucositis)[1]
- Central venous catheters[1]

SID: secondary immunodeficiency; HZ: Herpes Zoster; VZV: Varicella Zoster Virus

1. Nucci, M. and Anaissie, E., Clin Infect Dis. 2009; 49:1211-25, 2.Patel, S.Y. et al., Front Immunol. 2019; 10:33, 3. Ying L. et al. Oncotarget 2017; 8:46593-600, 4. Drgona, L. et al., Clin Microbiol Infect. 2018; 24:S83-94.

Infections in multiple myeloma patients treated with IMiDs

SECONDARY IMMUNE DEFICIENCY

IMiDs are new therapeutic agents that may be used for the treatment of MM, and have effects on the immune system different from conventional anti-MM treatments.

Infection rates:

- 16.6% rate of severe infection episodes after IMiD treatment in relapsed or refractory MM
- 10.5% rate of severe infection episodes in patients who received IMiD maintenance therapy after prior ASCT(s)

Treatment-specific infection risks:

- Risk of severe infections doubled in patients treated with lenalidomide as maintenance therapy, compared to those treated with thalidomide
- No increase in infection risk after IMiD-based maintenance therapy, compared with placebo or prednisolone treatment

ASCT: autologous stem cell transplant.

Girmenia, C. et al., Blood Rev. 2019; 34:84-94.

In Multiple Myeloma, numerous factors lead to infection risk and severity

SECONDARY IMMUNE DEFICIENCY

Underlying disease

Hypogammaglobulinaemia

Renal impairement

Treatment of underlying disease

Neutropaenia

Gastrointestinal Mucositis

Impaired cell-mediated immunity
Chemo- immunotherapy and immuno-suppressive therapy, steroids

Central Venous Catheter-related infections

HSCT

Patient-specific factors

Age-related frailty

Geriatric conditions

Organ dysfunction
Renal, heart and pulmonary impairment, gastrointestinal mucosa damage, diabetes

Physical and cognitive dysfunction

HSCT: haematopoietic stem cell transplantation.

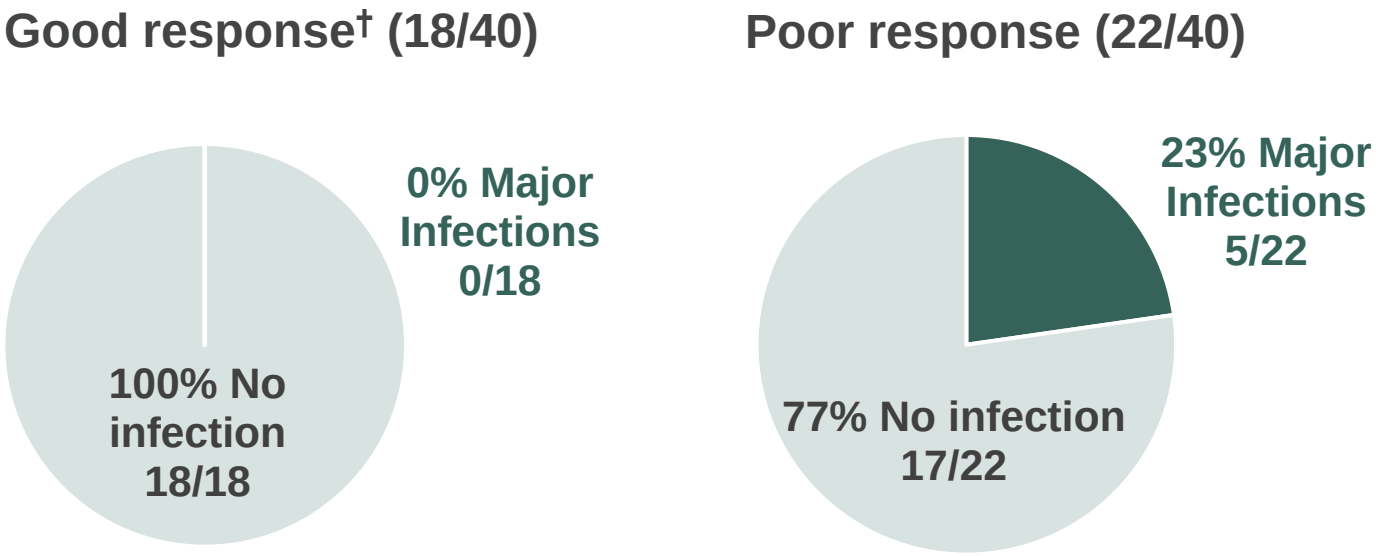
Blimark, C. et al., Haematologica, 2015;100:107; Nucci, M. et al., Clin Infect Dis., 2009;49:1211.

Major infections are associated with impaired immune response

SECONDARY IMMUNE DEFICIENCY

Infections in MM patients (all types) according to Pneumovax II* immunisation response**

N=40, p=0.03

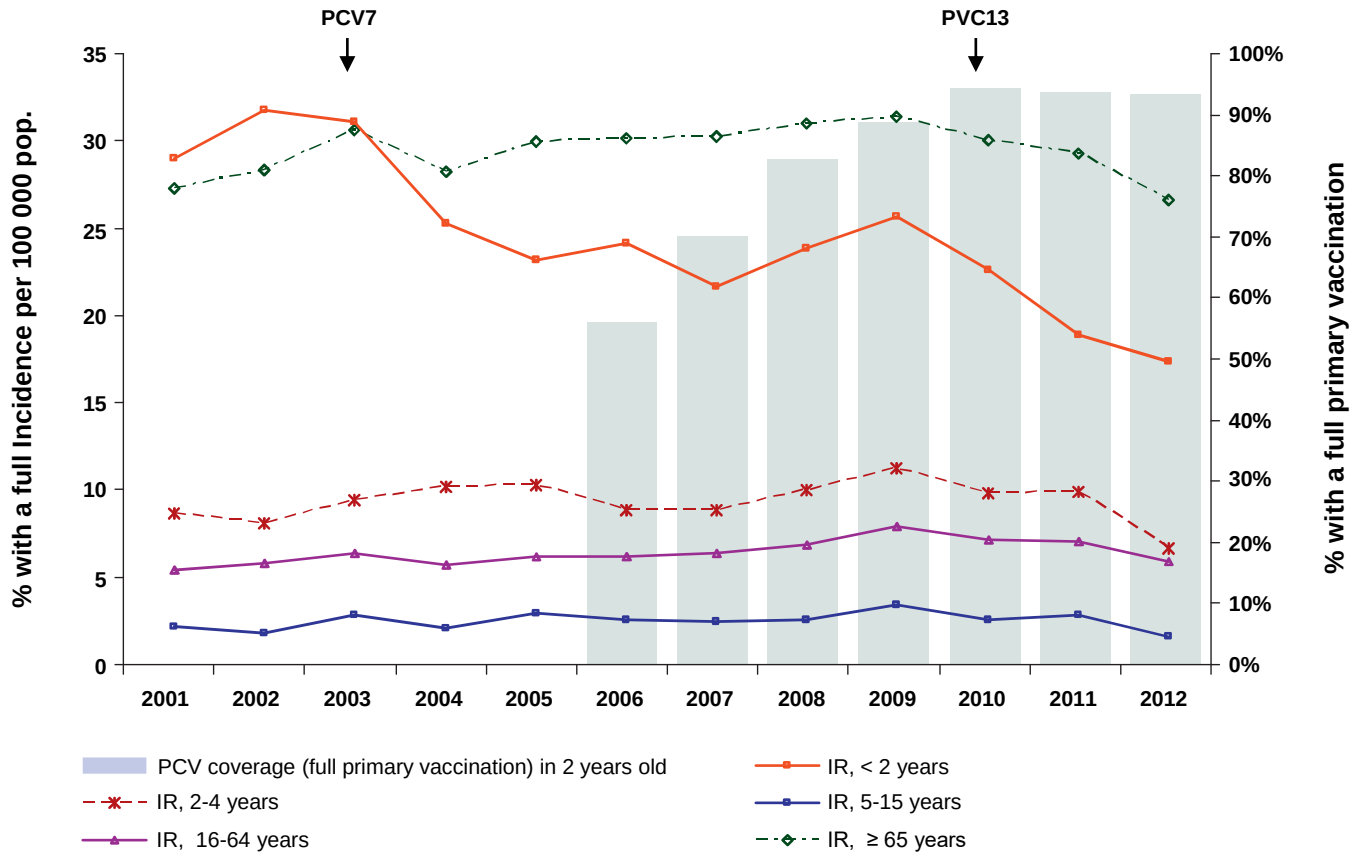


MM: multiple myeloma.
Infections were classified as Major in case of Septicaemia (culture positive), pyrexia of unknown origin (fever ≥39.5°C: culture negative), meningitis, Pneumonia (with X-ray evidence); as Moderate in case of upper respiratory tract infection complicated by secondary bacterial infection, acute bronchitis (not requiring hospital admission), pleurisy, urinary tract infection (culture positive or >100 pus cells/high power field), pyrexia of unknown origin (fever ≥ 38.5°C but <39.5°C: culture negative), skin abscess/cellulitis, localised herpes zoster; as minor in case of uncomplicated upper respiratory tract infection, minor skin infection, urinary tract infection (30-100 pus cells/high power field: culture negative).
Serious infections = major + moderate infections.
*Pneumovax II pneumococcal polysaccharide vaccine is recommended for immunisation against disease caused by pneumococcal serotypes contained in the vaccine.
†Good responders showed ≥2–fold increase of specific IgG titres as well as reaching minimum value based on normal range for age.**Immunisation responses were classified as poor, intermediate or good on the basis of the difference between the pre- and postimmunisation IgG antibody titres. Good responders showed an increase of at least twofold as well as a postimmunisation titre reaching a preset minimum value based on the normal range for age calculated from the baseline results obtained in the control population. Poor responders showed no difference between pre and postimmunisation titres; intermediate responders failed to produce an adequate enough response to be included in the good response group.
Hargreaves, R. M., et al., J Clin Pathol. 1995; 48:260-6, UK Medicines and Healthcare products Regulatory Agency, 2014, available at: https://www.gov.uk/drug-safety-update/pneumovax-ii-tolerability-of-re-vaccination

Would herd immunity also help reducing the infection risk of MM patients?

SECONDARY IMMUNE DEFICIENCY

Evolution of invasive pneumococcal diseases incidence rates (IR) by age-group and pneumococcal conjugated vaccines (PCV) coverage, France 2001–2012



Adapted from Lepoutre, et al. (2015) Vaccine, 33(2), 359–366.

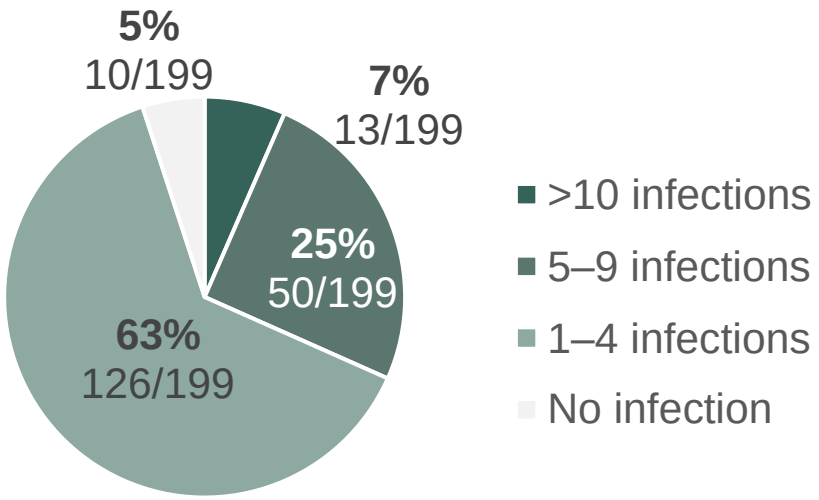
Infections frequently occur in Multiple Myeloma – Australian study

SECONDARY IMMUNE DEFICIENCY

Infections frequently occured in multiple myeloma patients

- 46% of MM patients had at least 1 infection
- 32% MM patient had frequent (>=5) and recurrent infections

Infection prevalence in patients with MM with 33-month follow-up (n=199)†



MM: multiple myeloma.

†Cumulative corticosteroid dose of >3200 mg over 2 months has the highest HR (3.06) for infections. The risk associated with 1–1600 mg and >1600–3200 mg cumulative corticosteroid doses over 2 months have HR of 1.39 and 1.97, respectively.

The median age of the patients included in the study was 63.8 years. Patients ISS stage was 1 (49.7%), 2 (37.2%), 3 (13.1%). As induction regimen, 38.7% of the patients received a thalidomide-based regimen, 26.1% a lenalidomide-based regimen, 18.6% a bortezomib based regimen, 15.1% a chemotherapy-based regimen and 2.0% received a regimen classified as «other». 78.9% of the patients received an ASCT, 2.5% an alloHCT and 18.6 % did not receive any stem cell transplant.

Teh, B.W. et al., Br J Haematol. 2015; 171:100-8.

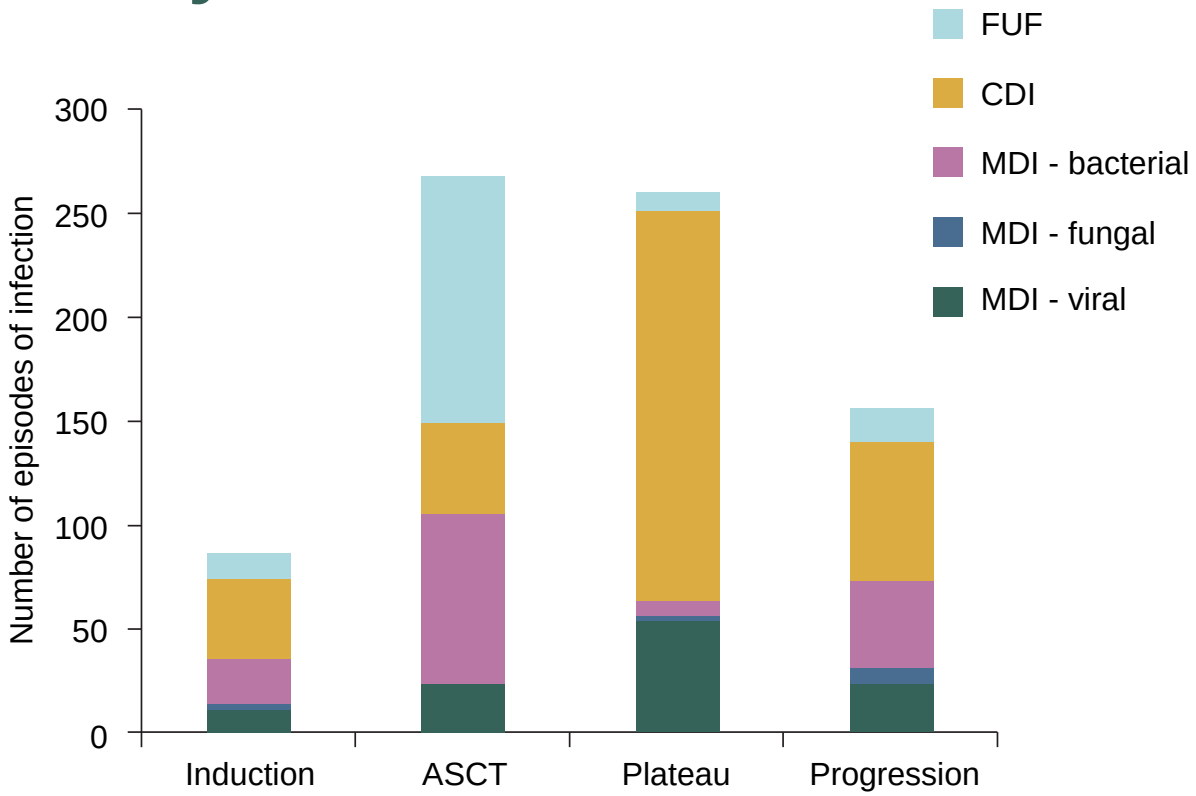
Epidemiology of infections in patients receiving an active treatment for MM - Australian study

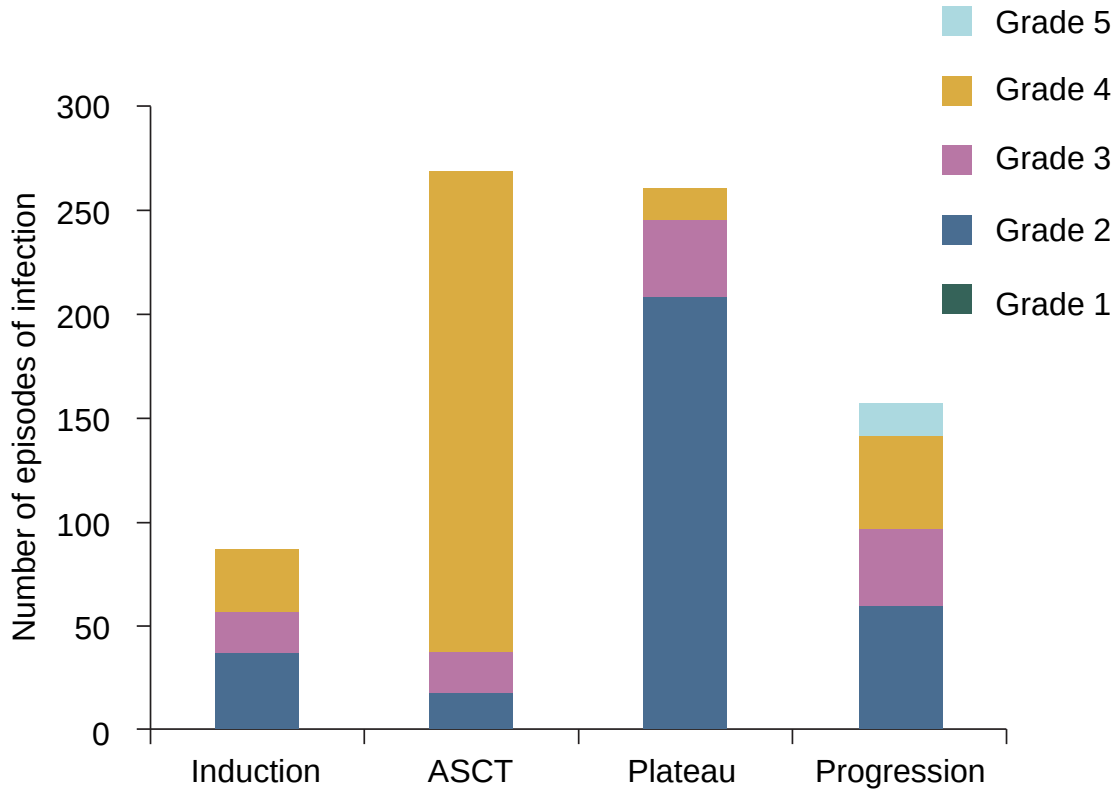
SECONDARY IMMUNE DEFICIENCY

- 199 MM patients with 771 episodes of infection (overall incidence of infection: 1.33 per patient-year)
- 43.7% of infections clinically defined, 36.4% microbiologically defined (bacterial - 54.1%, fungal - 5.7%, viral - 40.2%) and 19.8% were fever of unknown origin
- Bimodal peak in incidence of bacterial infections (4–6 and 70–72 months) and viral infections (7–9 and 52–54 months) from MM diagnosis
- Factors associated with increased risk of infection:
  - chemotherapy regimens (high-dose melphalan, intravenous cyclophosphamide, intensive combination systemic chemotherapy)
  - high-doses of corticosteroid
- Factors not independently associated with increased risk of infection: IMiDs and PI treatment

MM: multiple myeloma; IMiDs: immunomodulatory drugs; PI: proteasome inhibitors.
During a 33-month follow-up The median age of the patients included in the study was 63.8 years. Patients ISS stage was 1 (49.7%), 2 (37.2%), 3 (13.1%). As induction regimen, 38.7% of the patients received a thalidomide-based regimen, 26.1% a lenalidomide-based regimen, 18.6% a bortezomib based regimen, 15.1% a chemotherapy-based regimen and 2.0% received a regimen classified as «other». 78.9% of the patients received an ASCT, 2.5% an alloHCT and 18.6 % did not receive any stem cell transplant.
Teh, B.W. et al., Br J Haematol. 2015; 171:100-8.

Nature and severity of infections in patients with Multiple Myeloma across disease periods – Australian study





ASCT: autologous haematopoietic stem cell transplantation; MDI:microbiologically defined infections; CDI:clinically defined infections; FUF: fever of unknown origin.
During a 33-month follow-up. The median age of the patients included in the study was 63.8 years. Patients ISS stage was 1 (49.7%), 2 (37.2%), 3 (13.1%). As induction regimen, 38.7% of the patients received a thalidomide-based regimen, 26.1% a lenalidomide-based regimen, 18.6% a bortezomib based regimen, 15.1% a chemotherapy-based regimen and 2.0% received a regimen classified as «other». 78.9% of the patients received an ASCT, 2.5% an alloHCT and 18.6 % did not receive any stem cell transplant.

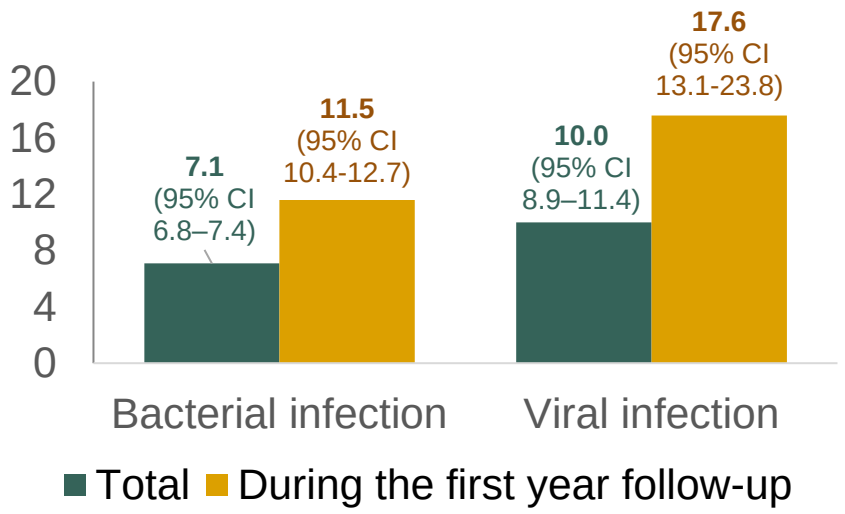
Teh, B.W. et al., Br J Haematol. 2015; 171:100-8.

Multiple Myeloma patients are at risk of bacterial and viral infection – a Swedish registry

SECONDARY IMMUNE DEFICIENCY

- Overall, multiple myeloma patients had a 7-fold increased risk of developing any infection vs matched controls
- The risk of all included infections was highest during the first year following MM diagnosis

Relative risk for bacterial and viral infection in MM patients compared with matched controls*



Patients' characteristics with MM and their matched controls

	Myeloma Patients	Matched Controls
Total, n (%)	9253 (100)	34,931 (100)
Sex, n (%)		
Male	4984 (53.9)	18,810 (53.9)
Female	4269 (46.1)	16,121 (46.1)
Age at dx, median (range)	72 (25-101)	72 (25-101)
Age group, n (%)		
Less than 40	77 (0.8)	299 (0.9)
40-49	381 (4.1)	1460 (4.2)
50-59	1062 (11.5)	4173 (12.0)
60-69	2169 (23.4)	8382 (24.0)
70-79	3423 (37.0)	12,917 (37.0)
80 and above	2141 (23.1)	7700 (22.0)
Year of diagnosis		
1988-1993	3247 (35.1)	12,214 (35.0)
1994-1999	3259 (35.2)	12,321 (35.3)
2000-2004	2747 (29.7)	10,396 (29.7)

MM: multiple myeloma; CI, confidence interval.

*Compared with healthy people of the same gender, age and country of residence.

Population-based data from Sweden to identify all multiple myeloma patients (n=9253) diagnosed from 1988 to 2004 with follow up to 2007 and 34,931 matched controls.

Bacterial infections were Pneumonia (HR 7.7), Osteomyelitis (HR 3.5), Septicaemia (HR 15.6), Pyelonephritis (HR 2.9), Cellulitis (HR 3.0), Meningitis (HR 16.6), Endocarditis (HR 5.3). Viral infections were Influenza (HR 6.1) and Herpes Zoster (HR 14.8)

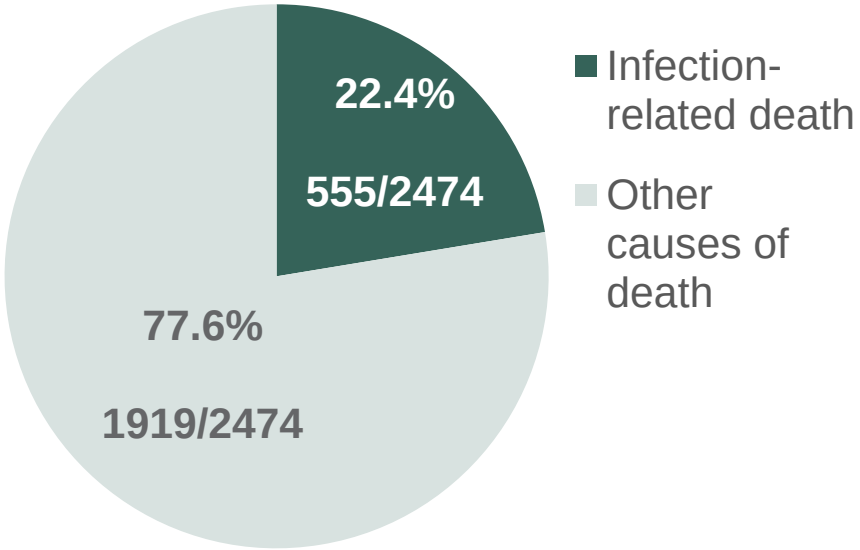
Note: No information about fungal infections.

Blimark, C. et al., Haematologica, 2015;100:107.

Infections are a substantial cause of death in Multiple Myeloma (all types) – a Swedish registry

- 22,4% of MM deaths were due to infections within 1 year of diagnosis
- The 3-year risk of death in infections in MM patients was 12.2% and the corresponding number for matched controls was 2.2%
- There was no change in risk of infection-related deaths according to age group (>65 and ≤65 years of age) over the three calendar periods
- Infection risk increased in the last decade potentially due to modern therapies

Infection-related death in MM (n=9,253) at 1 year of diagnosis



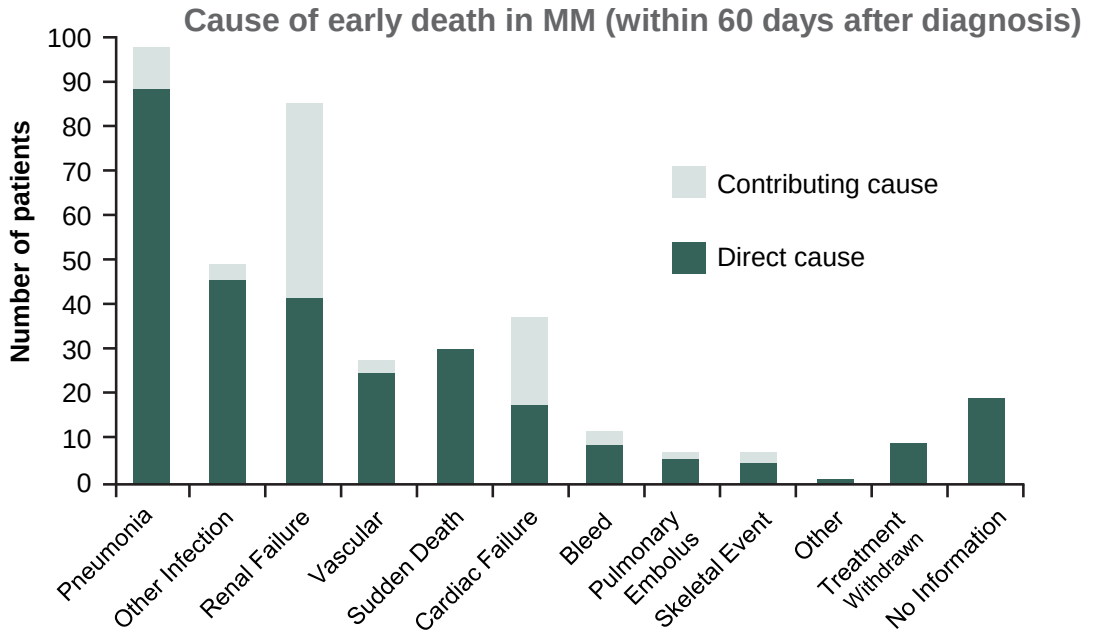
MM: multiple myeloma.
Population-based data from Sweden to identify all multiple myeloma patients (n=9253) diagnosed from 1988 to 2004 with follow up to 2007 and 34,931 matched controls. To assess the role of novel MM therapies in relation to the development of infections, patients were stratified to three calendar periods: 1988-1993, 1994-1999 and 2000-2004, reflecting time periods with different treatment strategies.
Blimark, C. et al., Haematologica, 2015;100:107

Early mortality after diagnosis of Multiple Myeloma – a UK analysis

- 5 Multiple Myeloma Medical Research Council Trials (1980 and 2002)
- 3,107 newly diagnosed patients
- Early death (within 60 days of diagnosis) - 299 patients (10%)
- Early death attributable to infection as direct cause - 45%

Trials characteristics

Trial	Total No. of patients	Age	Trial Dates	Induction Treatment	No. of Patients	Early Deaths No.	Early Deaths %
IVth	532	<80	1980-1982	MP	264	37	14
				MPV	268	28	10
Vth	691	<75	1982-1986	C-weekly plts < 80	61	8	13
				M7	316	44	14
				ABCM	314	33	11
VIth	712	<75	1986-1991	HDM (M140)	15	3	20
				HDMP	13	1	8
				ABCM	342	30	9
				ABCM-P	342	39	11
	299	<75	1991-1993	NR* ABCM	299	15	5
VIIth	405	<66	1993-2000	ABCM	202	8	4
				C-VAMP	203	9	4
VIIIth	468	>65 or < 65 if HDT contraindicated	1993-2002	ABCM to plateau	125	0	0
				ABCM X3 then C-weekly	119	0	0
				NR*	224	44	20
Total	3.107				3.107	299	10

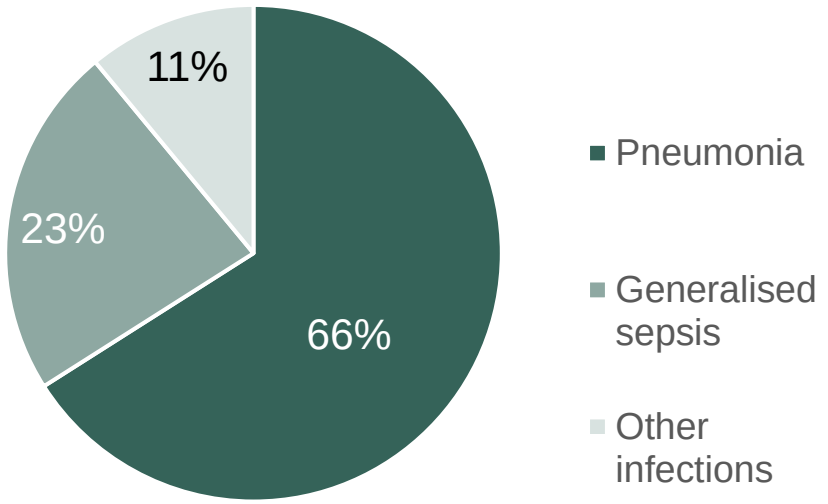


MRC: Medical Research Council; MP: melphalan prednisolone; MPV: melphalan prednisolone vincristine; C-weekly plts: cyclophosphamide weekly for low platelets; M7: melphalan; ABCM: doxorubicin, carmustine, cyclophosphamide, and melphalan; NR, nonrandomized; C-VAMP: cyclophosphamide vincristine doxorubicin methylprednisolone; HDT, high dose therapy.
*Indicates nonrandomized patients.
Review of early deaths in multiple myeloma in a serie of large trials to assess direct causes of death, their predictability, and whether current management strategies have reduced their frequency.
Augustson, B. M. et al., J Clin Oncol., 2005;23:9219.

Infections led to early death in Multiple Myeloma – a UK analysis

- Fatal bacterial infection were mainly pneumonia (66%) and generalised sepsis (23%)

Types of fatal bacterial infections (n=89)*



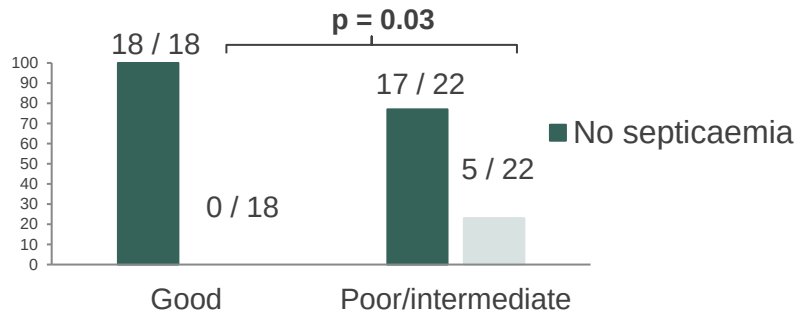
MM, multiple myeloma.
Review of early deaths in multiple myeloma in a serie of large trials to assess direct causes of death, their predictability, and whether current management strategies have reduced their frequency.
*Death within 60 days of trial entry occurred in 299/3107 (10%) of patients.
Augustson, B. M. et al., J Clin Oncol., 2005;23:9219.

Impaired response to immunisation in multiple myeloma is associated with increased risk of a major infection

SECONDARY IMMUNE DEFICIENCY

- Response to immunisation in plateau-phase MM patients may identify those at risk of infection.[1]
- A prospective study in the UK followed 102 patients with MM for a mean duration of 10 months.[1] Patients in plateau phase were immunised with Pneumovax II (n = 40)[1], a pneumococcal polysaccharide vaccine.[#2] Patients were classified by their immune response.*[1]
- MM patients with a poor/intermediate immunisation response to Pneumovax II had a higher frequency of septicaemia.[1]

Incidence of septicaemia in MM patients in plateau phase (n = 40)[1]



Of the 18 patients who showed a good response to immunisation, none had a septicaemic episode recorded since diagnosis of MM.

Of the 22 patients with a poor/intermediate immunisation response, 22.7% of patients had a septicaemic episode recorded since diagnosis of MM

[#] Pneumovax II is a pneumococcal polysaccharide vaccine recommended for immunisation against disease caused by pneumococcal serotypes contained in the vaccine.
*Immunisation responses, based on differences between pre- and post-immunisation IgG titres, were classified as: Good: ≥ 2-fold increase of specific IgG titres as well as the post-immunisation titre reaching the minimum of the normal range for age (calculated from the baseline results obtained in the control population); Poor: no difference between pre- and post-immunisation titres; Intermediate: inadequate response for inclusion in the good response group.

1. Hargreaves, R. M., et al., J Clin Pathol. 1995; 48:260-6, 2. UK Medicines and Healthcare products Regulatory Agency, 2014, available at: https://www.gov.uk/drug-safety-update/pneumovax-ii-tolerability-of-re-vaccination

Management of infectious complications in MM - Expert panel consensus-based recommendations

SECONDARY IMMUNE DEFICIENCY

- Careful evaluation of performance status and past medical history
- The quantitative evaluation of serum polyclonal immunoglobulins, absolute lymphocytes count, and the absolute neutrophil count to define the individual risk of infections
- Information on recent vaccination history - define the pre-treatment vaccination schedule
- HBV and HCV screening
- Colonisation screening in candidates to ASCT and undergoing intensive salvage therapy
- **Severe active infections** (i.e. pneumonia, herpes zoster, HBV or HCV related hepatitis, CMV disease, tuberculosis or HIV-disease **contraindicate therapies** in MM until their complete resolution or control

MM: multiple myeloma; HBV: Hepatitis B virus; HCV: Hepatitis C virus; ASCT: autologous stem cell transplant; CMV: cytomegalovirus.
Girmenia, C. et al., Blood Rev. 2019; 34:84-94.

Expert panel consensus-based recommendations in MM - Antibacterial prophylaxis

- Antibacterial prophylaxis (ciprofloxacin 500 mg bid; levofloxacin 500 mg *od*) during the first few months particularly in patients receiving IMIDs and in those at high risk of infections
- In patients with neutropaenia on lenalidomide-based maintenance therapy fluroquinolone prophylaxis may be considered
- Fluoroquinolone prophylaxis from day 5 until stable neutrophil engraftment after ASCT
- Fluoroquinolone prophylaxis in patients with relapsed/refractory (R/R) disease with treatment - related prolonged neutropaenia

MM: multiple myeloma; bid: twice a day; ASCT: autologous stem cell transplant; R/R: relapsed / refractory.

Girmenia, C. et al., Blood Rev. 2019; 34:84-94.

Expert panel consensus-based recommendations in MM - Antifungal prophylaxis

SECONDARY IMMUNE DEFICIENCY

- Candida prophylaxis (fluconazole 400 mg od or micafungin 50 mg *od*) considered after ASCT in patients with oral mucositis
- Prophylaxis against PJP recommended during PIs therapy, prolonged steroid treatment, R/R disease and after engraftment in ASCT
  - trimethoprim-sulphamethoxazole (160/800 mg *bid* for 2 or 3 days/week- the first choice
  - alternative agents - aerosolized pentamidine (300 mg once/month), dapsone (50 mg×2/day) and atovaquone (1500 mg/day)

MM: multiple myeloma; ASCT: autologous stem cell transplant; R/R: relapsed/refractory; PJP: *Pneumocystis jirovecii* pneumonia; PI: proteasome-inhibitors
Girmenia, C. et al., Blood Rev. 2019; 34:84-94.

Expert panel consensus-based recommendations in MM - Antiviral prophylaxis

SECONDARY IMMUNE DEFICIENCY

- HZ and HSV infection – acyclovir (5 mg/kg q12h i.v. or 3×200 mg/d to 2x800mg/d p.o.) or valaciclovir (500 to 3×500 mg/d p.o.) during PIs therapy, recent history of HZ, severe/recurrent HSV infection and following ASCT
- Chronic HBV infection - tenofovir or entecavir, resolved HBV infection - lamivudine
- HCV-infected patients receiving chemotherapy - monitoring of liver function tests and HCV RNA - in HCV RNA positive patients antiviral treatment according to the specific indication
- IVIG is not recommended routinely for patients with MM
- The use of IVIG may be reserved to patients with very low IgG levels (< 400 mg/dl) and recurrent life-threatening infections

HZ: Herpes Zoster; HSV: Herpes Simples Virus; PI: proteasome inhibitor; ASCT: autologous stem cell transplant; HBV: Hepatitis B virus; HCV: hepatitis C virus; RNA: ribonucleic acid; MM: multiple myeloma; IVIG: intravenous immunoglobulin.

Girmenia, C. et al., Blood Rev. 2019; 34:84-94.

Expert consensus-based recommendations for immunoglobulin replacement therapy in haematological malignancies

SECONDARY IMMUNE DEFICIENCY

- In patients with haematological malignancies who suffer from severe, recurrent or persistent infections despite appropriate anti-infective treatment, IgRT should be considered if IgG levels are < 4 g/L **or** if test immunisation has failed[#].
- In patients with haematological malignancies who suffer from persistent, recurrent or severe infections despite appropriate anti-infective treatment, **test immunisation*** could be a tool to help decide if IgRT should be initiated, particularly in patients whose serum Ig levels do not reflect the functional status of their immune system
- When initiating IgRT to prevent infections, discontinuing anti-infective treatment can be considered when infection burden has been reduced, unless it is warranted by specific risk factors or other complications.

[#] not achieving a two-fold rise in specific antibody levels
* polysaccharide and polypeptide pneumococcal vaccines
Ig: immunoglobulin; IgG: immunoglobulin G; IgRT: immunoglobulin replacement therapy

Jolles, S. et al., Eur J Haematol. 2021; DOI: 10.1111/ejh.13580

Expert consensus-based recommendations for immunoglobulin replacement therapy in haematological malignancies

SECONDARY IMMUNE DEFICIENCY

- IgRT is generally **well tolerated** in patients with haematological malignancies. IgRT can on rare occasions lead to adverse events such as hypersensitivity, renal failure, thromboembolism and haemolysis. IVIg administration should be closely monitored, particularly in patients with risk factors. Adequate hydration is important. **SCIg administration might present a lower risk of systemic adverse events.**
- The subcutaneous administration of Ig induces fewer systemic side-effects, allows **more stable Ig trough levels** and the self-administration of Ig at home may offer **quality-of-life benefits** to patients wishing to self-infuse. All patients with haematological malignancies whose secondary immunodeficiency requires IgRT should have access to SCIg as a treatment option.

IgRT: immunoglobulin replacement therapy; IVIg: intravenous immunoglobulin; SCIg: subcutaneous immunoglobulin

Jolles, S. et al., Eur J Haematol. 2021; DOI: 10.1111/ejh.13580

Expert consensus-based recommendations for immunoglobulin replacement therapy in haematological malignancies

SECONDARY IMMUNE DEFICIENCY

- In patients with HM and in patients undergoing HSCT, the minimum IgG maintenance dose should be **0.4 g/kg body weight over a 3 to 4-week period**.
- In patients with HM who require IgRT, discontinuation should be considered after a clinically significant period without infections or if there is evidence of immunological recovery*.
- In patients with HM who require IgRT, discontinuation should be considered after at least 6 months without infections and if there is evidence of immunological recovery*.
- In patients with HM whose IgRT is discontinued, infection rates should be closely monitored and IgG levels should be tested during routine patient visits.
- In patients with HM whose IgRT had been discontinued and severe or persistent infections recur, restarting IgRT should be the treatment of choice if hypogammaglobulinaemia is present.

*outside periods of high incidence of infectious diseases
HM: haematological malignancies; HSCT: haematopoietic stem cell transplantation; IgG: immunoglobulin G, IgRT: immunoglobulin replacement therapy

Jolles, S. et al., Eur J Haematol. 2021; DOI: 10.1111/ejh.13580

SECONDARY IMMUNE DEFICIENCY

Supported by

octapharma