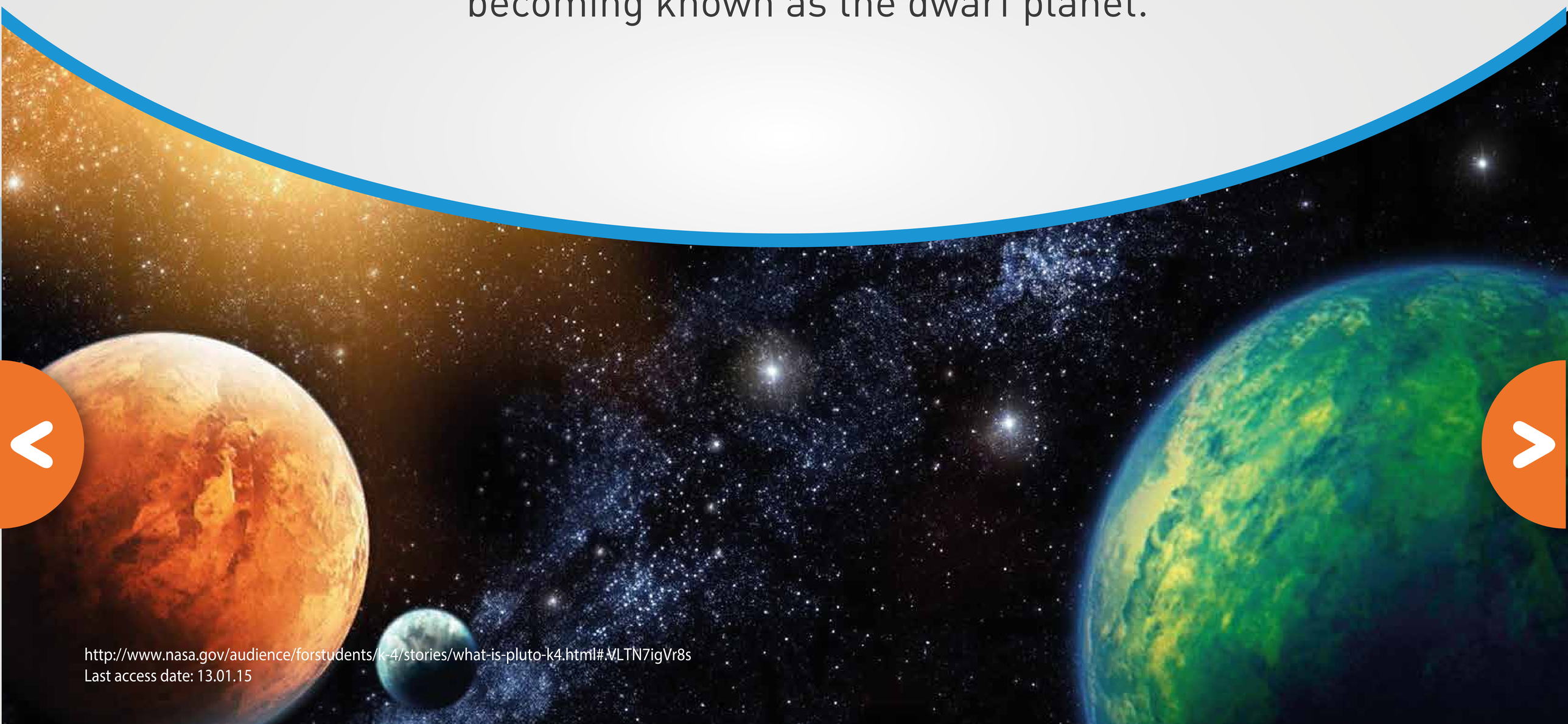
Why 8?

1 Why 8 planets?

1

Why 8 planets?

From 9 down to 8: Goodbye pluto!
Too small, too far from the sun,
becoming known as the dwarf planet.



http://www.nasa.gov/audience/forstudents/k-4/stories/what-is-pluto-k4.html#.VLTN7igVr8s
Last access date: 13.01.15

2 Why 8 cups of water/day?

2

Why 8 cups of water / day?

Back in 1945, the food and nutrition board of the national research council stated that adults should take in about 2.5 liters of water per day (which is roughly the equivalent of eight glasses of water)

http://www.colourlovers.com/blog/2010/01/25/all-the-colors-of-the-rainbow
Last access date: 13.01.15

3 Why 8 working hours?

< >

3

Why 8 working hours?

A major throwback to the 18th century:
10-16 hrs was the norm.
Thank you Robert Owen for your successful campaign, making them 8 hrs/day.

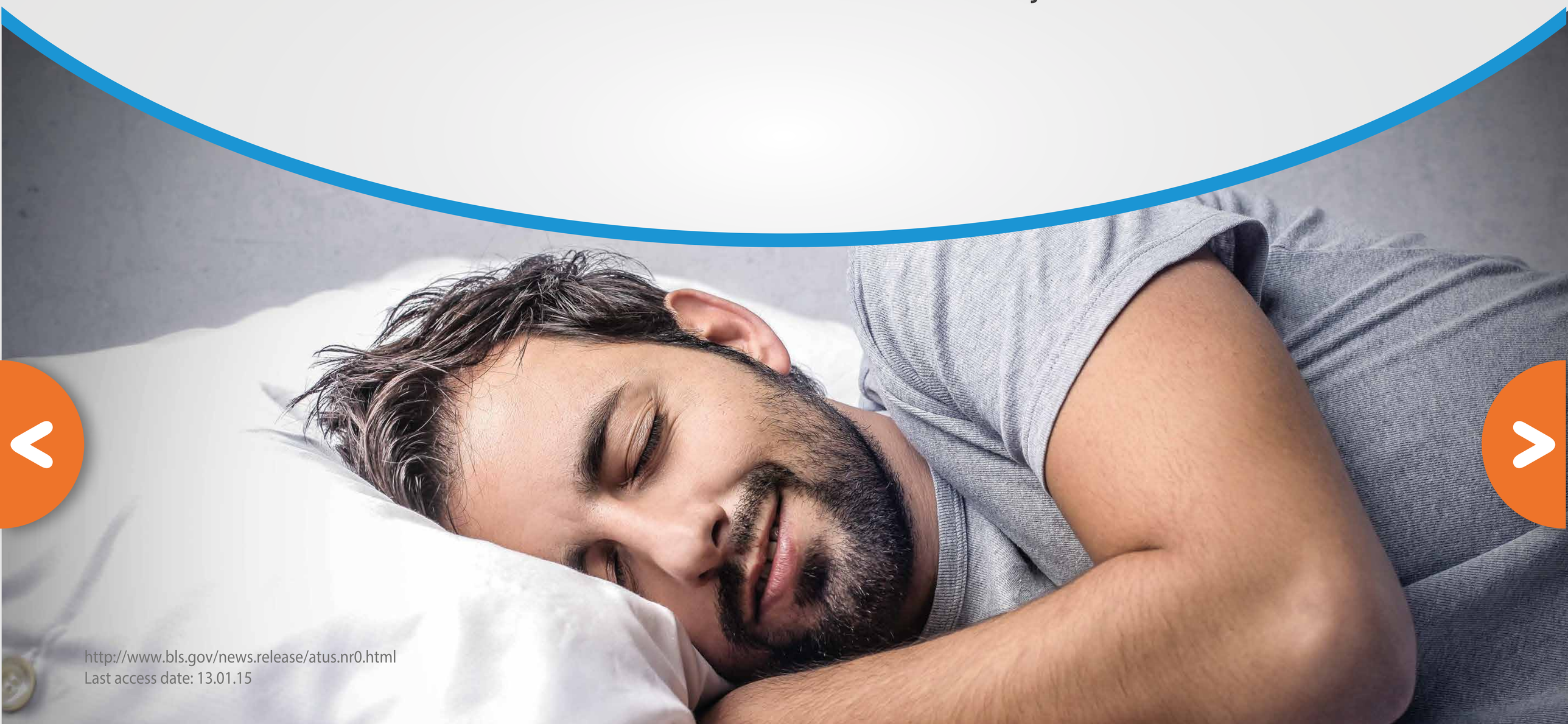
http://www.huffingtonpost.com/leonhard-widrich/the-origin-of-the-8-hour-_b_4524488.html
Last access date: 13.01.15

4 Why 8 hours of sleeping /day?

4

Why 8 hours of sleeping / day?

A survey was conducted, with results reporting that young adults slept an average of 8 hours.
Let’s face it - we all need to dream every now and then!



http://www.bls.gov/news.release/atus.nr0.html
Last access date: 13.01.15

5 Why the 8th tooth is called wisdom tooth?

5

Why the 8th tooth is called wisdom tooth?

Because it appears much later than the other teeth, usually between the ages of 17 and 25 when a person reaches adulthood. For the majority, it needs to be extracted: too much wisdom to handle!

http://www.drdainiusrazukevicius.com/en/eight-wisdom-teeth-extraction/
Last access date: 13.01.15

6 Why g8?

6

Why g8?

The group of eight was the name of a forum for the governments of a group of eight leading industrialized countries: Canada, France, Germany, Italy, Japan, Russia, U.K & U.S.

http://www.g8.co.uk/
Last access date: 13.01.15

7 Why 8 colors?

7

Why 8 colors?

There are 8 colors in a rainbow: red, orange, yellow, green, teal, cyan, blue, purple.

>

http://www.colourlovers.com/blog/2010/01/25/all-the-colors-of-the-rainbow
Last access date: 13.01.15

8

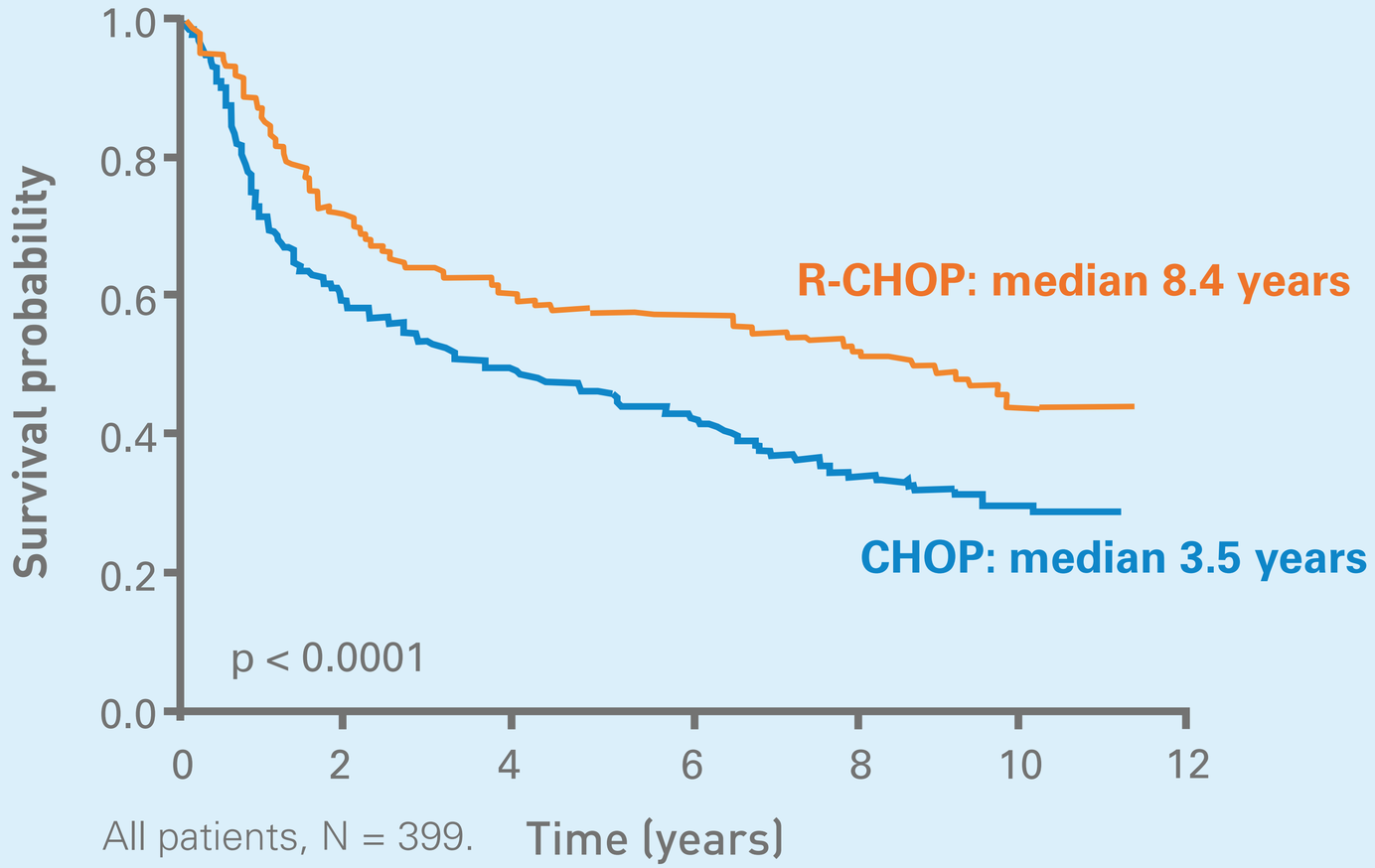
Why 8 cycles of **MabThera** in DLBCL?

Because in DLBCL, CURE is the GOAL

MabThera®
Rituximab
CENTRAL TO SUCCESS

Why 8 cycles of **MabThera** in DLBCL?

Because **8 MabThera** + CHOP delivers 8.4 yrs OS in the GELA LNH-98.5:



All patients, N = 399.

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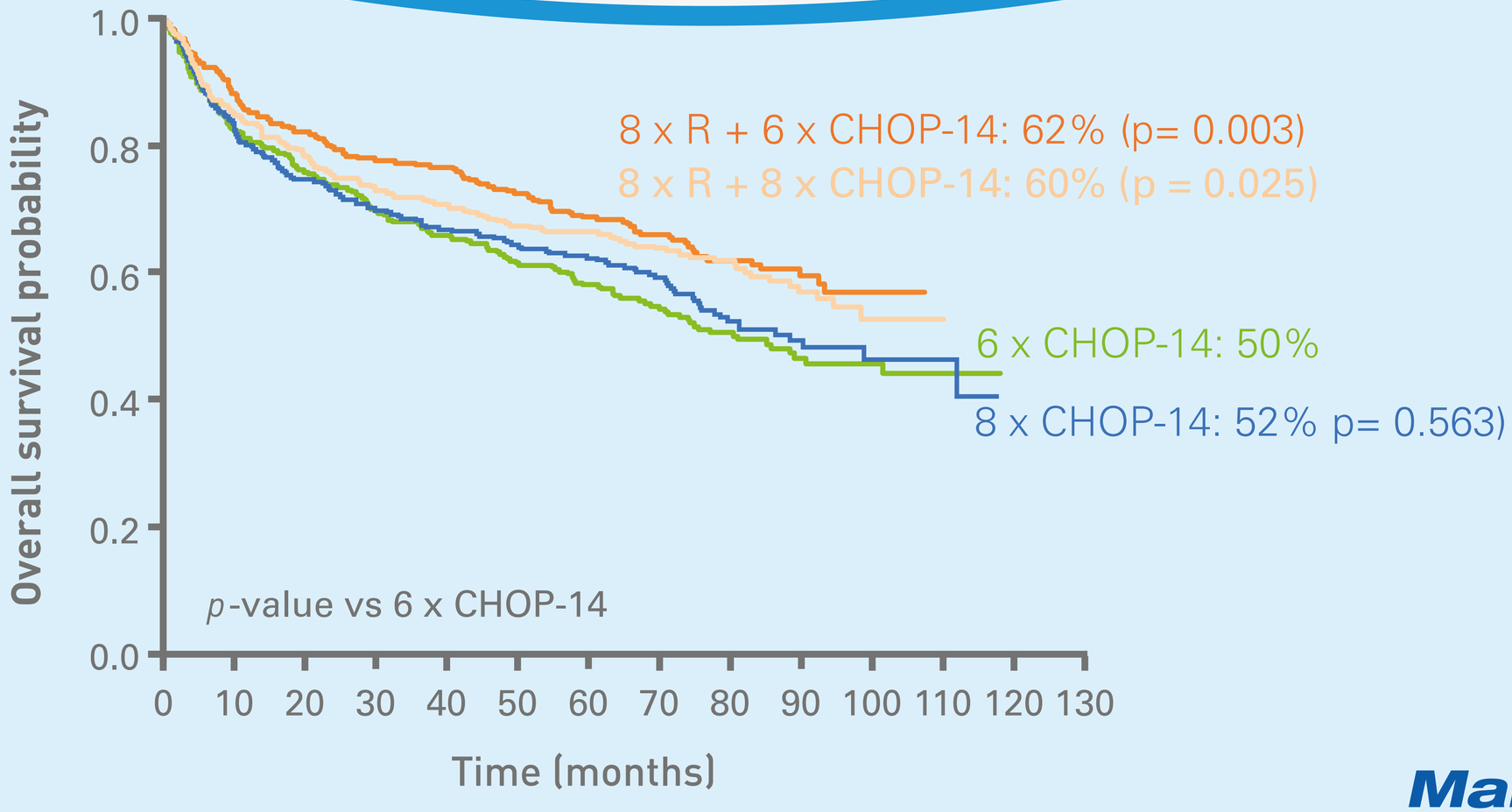
Coiffier B, et al. Blood 2010; 116:2040 – 2045.

Why 8 cycles of **MabThera** in DLBCL?

Because **8 MabThera** +6-8 CHOP improves 7- year OS in the RiCOVER-60



Pfreundschuh M, et al. J Clin Oncol 2011; 29 (Suppl): Abstract 8029. Poster presentation.

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Why 8 cycles of **MabThera** in DLBCL?

Because **8 MabThera** + chemo improves
EFS and OS in the GELA LNH03-2B

Outcome	R-CHOP	R-ACVBP	HR	p-value
3-year EFS	67%	81%	0.56	0.0035
3-year PFS	73%	87%	0.48	0.0015
3-year overall survival	84%	92%	0.44	0.0071

- **MabThera** plus dose-intensive ACVBP shows improved survival in young, low-intermediate risk DLBCL patients

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Récher C, et al. Lancet 2011; 378:1858–1867.

Why 8 cycles of **MabThera** in DLBCL?

Because **8 MabThera** in DLBCL has an
Accumulating evidence

Study	Regimen	Outcome	p value
GELA LNH-98.5[1] (60–80 yrs)	8 x R-CHOP-21	mPFS: 4.8 yrs	0.0001
	8 x CHOP-21	mPFS: 1.2 yrs	
RiCOVER-60[2,3] (61–80 yrs)	8 x R + 6 x CHOP-14	7-yr EFS: 50%	0.001
	6 x CHOP-14	7-yr EFS: 33%	
	8 x R + 8 x CHOP-14	7-yr EFS: 52%	NA
	8 x CHOP-14	7-yr EFS: 40%	
GELA LNH03-2B[4] (18–59 yrs)	8 x R + 4 x ACVBP-14	3-yr EFS: 81%	0.0035
	8 x R-CHOP-21	3-yr EFS: 67%	
Cunningham et al.[5]	8 x R + 8 x CHOP-21	PFS hazard ratio: 1.0 OS hazard ratio: 0.96	0.98 0.75
	8 X R + 6 x CHOP-14		

1. Coiffier B, et al. Blood 2010; 116:2040–2045. **2.** Pfreundschuh M, et al. Lancet Oncol 2008; 9:105 – 116.
3. Pfreundschuh M, et al. J Clin Oncol 2011; 29(Suppl):Abstract 8029. Poster presentation.
4. Récher C, et al. Lancet 2011; 378:1858–1867. **5.** Cunningham D, et al J Clin Oncol 2011; 29:Abstract 8000.

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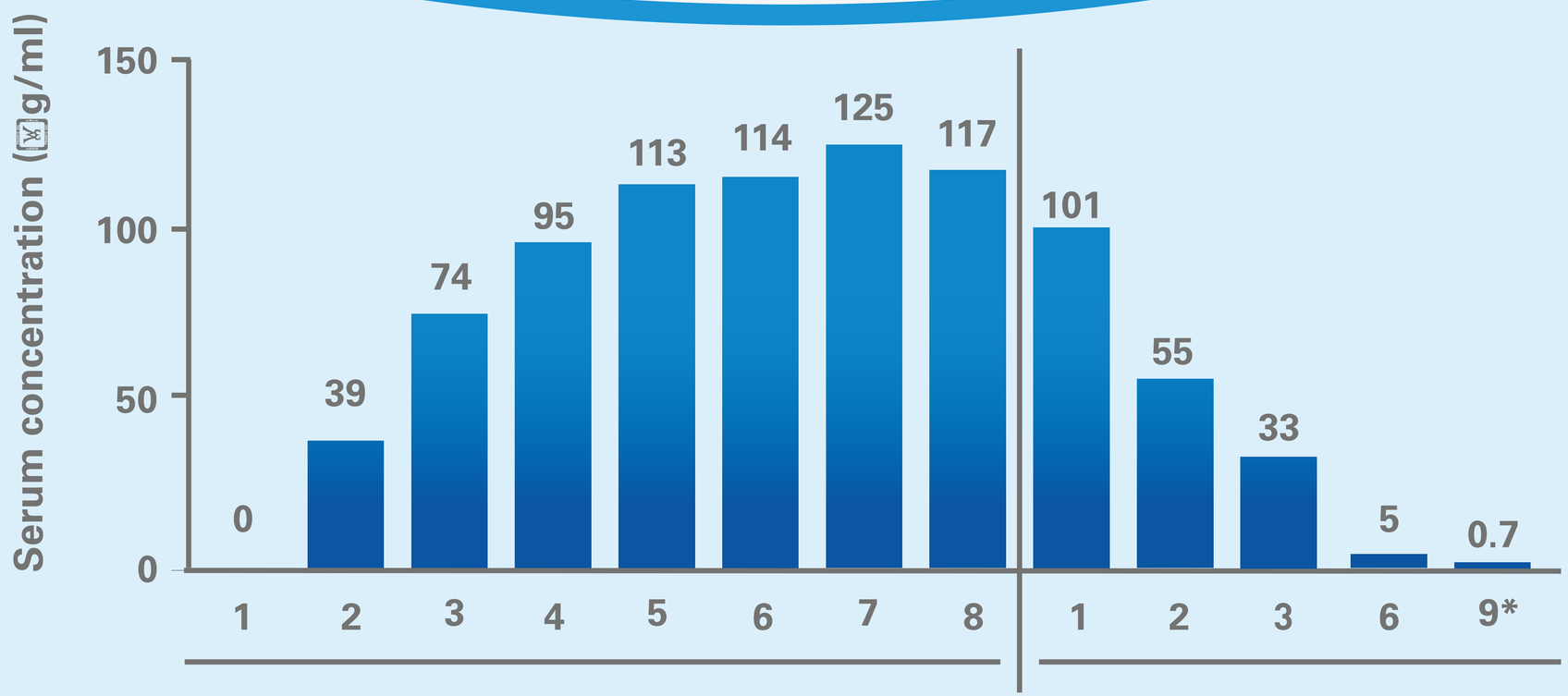
Why 8 cycles of **MabThera** in DLBCL?

Because Peak **MabThera** concentration
is not reached until cycle 7



* 7 patients evaluable after 9 months of treatment with 4/7 showing detectable MabThera levels.

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CENTRAL TO SUCCESS

Reiser M, et al. J Clin Oncol 2006; 24:Abstract 7537. Reiser M, et al. Blood 2006; 108: Abstract 2748.

Why 8 cycles of **MabThera** in DLBCL?

8 MabThera is the approved schedule in the EU and US[1,2] and is recommended for the majority of DLBCL patients by the ESMO guidelines[3]

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1. MabThera SmPC. **2.** RITUXAN Prescribing Information **3.** ESMO Guidelines 2012

Why 8 cycles of **MabThera** in DLBCL?

Because EXPERTS say

Intensive therapy with curative intent should be given to all [DLBCL] patients who can tolerate such therapy"

(Paul Fields and David Linch)[1]

"DLBCL is still curable"

(Michael Pfreundschuh)[5]

"DLBCL is a chemotherapy-curable lymphoma"

(James Armitage and Dennis Weisenburger)[2]

"More than 50% of elderly DLBCL patients can be expected to be cured by modern immunochemotherapy [R-CHOP]"

(Michael Pfreundschuh)[4]

"[Results of the 10-year follow-up of the GELA study] underscore the need to treat elderly patients as young patients, with the use of curative chemotherapy"

(Bertrand Coiffier)[3]

1. Fields PA & Linch DC. Br J Haematol 2012; 157:159 –170. **2.** Armitage JO & Weisenburger DD. J Clin Oncol 1998; 16: 2780–2795. **3.** Coiffier B, et al. Blood 2010; 116:2040 – 2045. **4.** Pfreundschuh M. Blood 2010; 116:5103-5110. **5.** Pfreundschuh M & Schwaner I. Medical Tribune Oncology Hematology 2011; 2121.

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SIMPLY BECAUSE

8 MabThera + Chemotherapy is the standard of care[1,3] that offers the best chance of CURE for YOUR DLBCL PATIENT[4,7].

1. MabThera SmPC **2.**Rituxan Prescribing Information **3.** ESMO Guidelines **4.**Coiffier B, et al. Blood 2010; 116:2040-2045. Long-term outcomes of patients in the LNH-98.5 trial **5.** Coiffier B, et al. N Engl J Med 2002;346:235-242 **6.** Pfreundschuh M, et al. Lancet Oncol 2008; 9:105-116 **7.** Pfreundschuh M, et al. J Clin Oncol 2011;29(Suppl):Abstract 8029. Poster presentation

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Why 8 cycles of **MabThera** in DLBCL?

Abbreviated Prescribing information MABTHERA®
Indications: ***Oncology***: (i) Monotherapy in patients with CD20-positive follicular non-Hodgkin's lymphoma (stage III–IV) who have relapsed after, or failed to respond to, chemotherapy. (ii) Treatment of previously untreated patients with CD20-positive follicular non-Hodgkin's lymphoma (stage III–IV) with high tumor burden in combination with CVP or CHOP. Responders may be administered maintenance therapy with rituximab monotherapy for 2 years.(iii) Maintenance therapy of patients with relapsed or refractory CD20-positive follicular non-Hodgkin's lymphoma (stage III–IV) who have responded to induction therapy with CHOP with or without rituximab. (iv) Treatment of patients with CD20-positive diffuse large B cell non-Hodgkin's lymphoma (DLBCL) in combination with standard CHOP (8 cycles of cyclophosphamide, doxorubicin, vincristine and prednisone). (v)Use in combination with fludarabine and cyclophosphamide (R-FC) for patients requiring treatment for chronic lymphocytic leukemia (CLL). Patients previously treated with fludarabine should have responded for a period of at least 6 months. ***Rheumatoid Arthritis:*** MabThera in combination with methotrexate is indicated in adult patients for the treatment of moderate to severe, active rheumatoid arthritis in patients with an inadequate response or intolerance to one or more tumour necrosis factor inhibitor therapies. MabThera has been shown to reduce the rate of progression of joint damage as measured by x-ray, to improve physical function and to induce major clinical response, when given in combination with methotrexate. ***ANCA-associated vasculitis (AAV):*** MabThera is indicated in combination with corticosteroids for the treatment of patients with severe active ANCA-associated vasculitis (granulomatosis with polyangiitis [also known as Wegener's granulomatosis] and microscopic polyangiitis). ***Dosage and Administration: Oncology:*** Administer prepared MabThera as IV infusion through a dedicated line, with full resuscitation facilities immediately available and under supervision of an experienced physician. Do not administer as IV push or bolus. Administer premedication (eg an anti-pyretic and an antihistamine) before each infusion. Consider premedication with glucocorticoids, if not given in combination with a glucocorticoid-containing chemotherapy. Monitor closely for onset of cytokine release syndrome (CRS). Severe reactions e.g. severe dyspnoea, bronchospasm or hypoxia requires immediate interruption of infusion. Only restart infusion if symptoms resolve, at half previous rate. ***Diffuse large B-cell non-Hodgkin's lymphoma:*** In combination with CHOP, 375mg/m2 on day 1 of each chemotherapy cycle for 8 cycles, after the glucocorticoid component of CHOP. ***Follicular lymphoma:*** The recommended dosage of MabThera in combination with CVP or CHOP chemotherapy is 375 mg/m2 body surface area once per cycle for 8 treatment cycles. The dose of MabThera is given on day 1 of each chemotherapy cycle after oral administration of the glucocorticoid component of the chemotherapy. Maintenance : (i) In untreated patients MabThera is administered every 2 months (375 mg/m2 body surface area),(ii) In the treatment of recurrence MabThera is administered every 3 months (375 mg/m2 body surface area),(iii) The maintenance dose should be given until disease progression or for a maximum duration of two years. Chronic lymphocytic leukaemia: In combination with chemotherapy 375 mg/m2 administered on day 1 of the first treatment cycle followed by 500 mg/m2 administered on day 1 of each subsequent cycle for 6 cycles in total. Chemotherapy to be given after MabThera infusion. Prophylaxis with adequate hydration and administration of uricostatics starting 48 hours prior to start of therapy is recommended for CLL patients to reduce the risk of tumour lysis syndrome. For CLL patients whose lymphocyte counts are > 25 x 109/L it is recommended to administer prednisone/prednisolone 100 mg intravenous shortly before infusion with MabThera to decrease the rate and severity of acute infusion reactions and/or cytokine release syndrome. First Infusion: Recommended initial rate is 50mg/hr; after the first 30 minutes increase by 50mg/hr every 30 minutes to maximum of 400 mg/hr. Subsequent Infusions: Initial rate 100mg/hr; increase by 100mg/hr every 30 minutes to a maximum of 400mg/hr. Dose adjustments: No dose reductions of MabThera recommended. Apply standard dose reductions to chemotherapy agents in combination with MabThera. Rheumatoid Arthritis: The recommended dosage of MabThera is 1000 mg by IV infusion followed two weeks later by the second 1000 mg IV infusion. The need for further courses should be evaluated 24 weeks following the previous course with retreatment given based on residual or disease activity returning to a level above DAS28-ESR of 2.6 (treatment to remission). Patients may receive further courses no sooner than 16 weeks following the previous course. Patients should receive 100 mg IV methylprednisolone to be completed 30 minutes prior to both MabThera infusions to decrease the incidence and severity of infusion-related reactions. MabThera is not recommended in children. ***ANCA-associated vasculitis:*** The recommended dosage of MabThera for the treatment of ANCA-associated vasculitis is 375 mg/m2 body surface area administered once weekly as an intravenous infusion for 4 weeks. For the treatment of severe vasculitis symptoms it is recommended that MabThera be combined with intravenous methylprednisolone 1,000 mg daily for 1 to 3 days, followed by oral prednisone 1 mg/kg body weight/day (not to exceed 80 mg/day and to be tapered as rapidly as possible according to clinical need) during and after treatment with MabThera. Contra-indications: Hypersensitivity to any component of this product or to murine proteins. Precautions: Use extreme caution and closely monitor first infusion when treating patients with ≥ 25x109/l circulating malignant cells or high tumour burden (higher risk of severe cytokine release syndrome (CRS)). Consider reduced rate for first infusion or a split dosing over two days during the first cycle. Severe CRS: may be associated with some features of tumour lysis syndrome e.g. hyperuricaemia, hyperkalaemia, hypocalcaemia, hypophosphataemia, acute renal failure, elevated LDH and may be associated with acute respiratory failure and death. If severe CRS manifests stop infusion immediately and start aggressive symptomatic treatment. See SPC for full details. Anaphylaxis and other hypersensitivity reactions have been reported following IV administration of proteins to patients. Hypotension may occur during MabThera infusion; consider withholding anti-hypertensive medications 12 hours prior to infusion. Caution in patients with a history of pulmonary insufficiency, those with pulmonary tumour infiltration and patients with history of cardiac disease and/or cardiotoxic chemotherapy. Experience in patients with neutrophils <1.5 x 109/l and/or platelet counts <75 x 109/l is limited therefore use caution. Do regular full blood counts (FBC) when MabThera is given in combination with chemotherapy; consider periodic FBC during monotherapy. MabThera should not be administered to patients with an active and/or severe infection (e.g. tuberculosis, sepsis and opportunistic infections). Carefully monitor patients with history of hepatitis B infection for active infection when MabThera is used with chemotherapy. Consider differential diagnosis of Progressive Multifocal Leucoencephalopathy (PML) in patients reporting neurological symptoms. Safety or efficacy of immunization with any vaccine has not been studied. Drug interactions: Limited data available on possible drug interactions with MabThera. Patients with human antimouse antibody/human anti-chimeric antibody (HAMA/HACA) titres may have allergic or hypersensitivity reactions when treated with other monoclonal antibodies. Pregnancy and lactation: No adequate data from use in pregnant women. Do not give MabThera to a pregnant woman unless the potential benefit outweighs the risk. May cause B cell depletion in the foetus. Effective contraception required in women of childbearing age during and for up to 12 months following MabThera therapy. Women should not breastfeed during, and for 12 months following, MabThera therapy. Undesirable effects: Monotherapy: Common adverse reactions: Infusion related effects, observed in over 50% of patients on monotherapy, predominantly during first infusion, usually in first 2 hours; mainly fever, chills and rigors; other symptoms include flushing, angioedema, nausea, urticaria/rash, fatigue, headache, throat irritation, rhinitis, vomiting and tumour pain; accompanied by hypotension and bronchospasm in about 10% of cases. Incidence of infusion related reactions decreases substantially with subsequent infusions. Infections: B-cell depletion occurs in 70-80% of patients but decreased serum immunoglobulins in only a minority of patients; bacterial, viral & fungal infections, including severe infections and sepsis, were reported in single-arm trials. Haematological adverse events: occurred in a minority of patients and usually mild and reversible. Severe (grade 3 and 4) events occurred: thrombocytopenia, neutropenia, severe anaemia, haemolytic anaemia, pure red cell aplasia. Cardiovascular events: exacerbation of pre-existing cardiac conditions such as angina pectoris, myocardial infarction, hypotension, hypertension, arrhythmia. Bulky disease: higher incidence of grade 3 and 4 adverse events. Serum sickness reported. When used in combination with chemotherapy: Similar adverse reactions occur as for monotherapy. In addition: DLBCL: Grade 3/4 adverse events, including grade 2 infections, reported at a ≥2% higher incidence with R-CHOP compared to CHOP alone were: bronchitis, herpes zoster, sinusitis, dyspnoea, shivering, hypertension, atrial fibrillation. FL: Grade 3/4 adverse events reported at a ≥2% higher incidence with R-CVP compared to CVP alone or with R-CHOP compared to CHOP alone were fatigue and neutropenia, nausea, constipation, neutropenia, febrile neutropenia, alopecia, hypersensitivity. Maintenance therapy: Grade 3/4 adverse events reported at a ≥2% higher incidence with maintenance therapy compared to observation were: respiratory tract infection, neutropenia, leucopenia, alopecia and cardiac disorders. CLL: overall incidence of grade ¾ infections was comparable between the treatment groups (R-FC, FC). Serious adverse reactions observed in post-marketing surveillance: Serious viral infection. Late neutropenia, pancytopenia, aplastic anaemia. Severe events in patients with prior cardiac condition or cardiotoxic chemotherapy, heart failure, myocardial infarction. Hearing loss. Severe vision loss. Multiorgan failure. Infusion related reactions, anaphylaxis, tumour lysis syndrome, cytokine release syndrome, serum sickness. Very rare cases of Hepatitis B reactivation, including fulminant hepatitis with fatal outcome. Progression of pre-existing Kaposi's sarcoma, mainly in patients with HIV. Cranial neuropathy, peripheral neuropathy, facial nerve palsy, loss of other senses. Renal failure. Bronchospasm, respiratory failure, pulmonary infiltrates, interstitial pneumonitis. Gastro-intestinal perforation. Severe bullous skin reactions, toxic epidermal necrolysis. Vasculitis (various types). Prescribers should consult the SPC in relation to other side-effects. Latest Update April 2014.

Full Prescribing Information is available upon request.
In case of any adverse event occurring with MabThera®, please forward details to fax number: 00961 1 992 664 or by email to: the beirut.safety_reporting.bs1@roche.com

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