MARGINAL ZONE B-CELL LYMPHOMA

Markus Raderer
Internal Medicine I, Oncology
Medical University Vienna
DISTRIBUTION OF LYMPHOMA SUBTYPES IN ADULTS*

*Tissue biopsies
MODEL OF B-NHL PATHOGENESIS

BASIC CONSIDERATIONS

Extranodal marginal zone B-cell-lymphoma of the mucosa-associated lymphoid tissue (MALT lymphoma) 7–8%

Splenic marginal zone lymphoma 0.6–2%

Nodal marginal zone lymphoma –1%

“…distinction between nodal and extranodal lymphoma is not simply one of anatomy”

“…certain gastric lymphomas recapitulate the features of the Peyer’s patch rather than lymph nodes…”

Peyer’s patch from terminal ileum composed of a cluster of B-cell follicles and related T-cell areas (T)

L, efferent lymphatics

Leukaemic MZL
Bone marrow and blood

Splenic MZL
Spleen
 +/- bone marrow
 +/- blood
 +/- Hilar splenic LNN
 +/- Liver

Nodal MZL
Peripheral LNN

Disseminated MZL
Spleen
 + Peripheral LNN
 + bone marrow
 + blood
 +/− other extranodal sites

Extranodal MZL
(MALT Lymphoma)
Extranodal localisations

1% NHL
7–8% NHL
1–2% NHL

MZL: RELATED CLINICAL ENTITIES?
EXTRANODAL MARGINAL ZONE B-CELL LYMPHOMA OF MALT

Cytologically heterogeneous: small, centrocyte-like, scattered blasts, varying amount of plasma cells

Light chain restriction

Infiltrate occupies MZ of reactive lymphoid follicles

Lymphoepithelial lesions

Immunohistochemistry: CD20+, CD5-, CD10-, CD23-, bcl6-, cyclin D1-
**NODAL MZL: DIAGNOSIS?**

Clinical presentation versus MALT lymphoma:

<table>
<thead>
<tr>
<th></th>
<th>nMZL: n=20</th>
<th>MALT: n=73</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage III/IV</td>
<td>71%</td>
<td>34%</td>
</tr>
<tr>
<td>Peripheral LNN</td>
<td>100%</td>
<td>8%</td>
</tr>
<tr>
<td>Para-aortal LNN</td>
<td>56%</td>
<td>14%</td>
</tr>
<tr>
<td>5-yr-OS</td>
<td>56%</td>
<td>81%</td>
</tr>
<tr>
<td>5-yr-FFS</td>
<td>28%</td>
<td>65%</td>
</tr>
</tbody>
</table>

PTPRD mutations are enriched in NMZL among mature B-cell tumours

Kaplan-Meier log-rank curves for CACNB2 (cg01805540), HTRA1 (cg25920792), and KLF4 (cg07309102) genes in test and validation cohorts. The 3 genes were significantly associated with OS in both cohorts (*p<0.05)²

TREATMENT STRATEGIES  SPLENIC MZL

R-monotherapy
Splenectomy
R-chemo?
Anti-HCV treatment

1.9 Consensus statement
Criteria for initiating treatment in SMZL are the following: [3] progressive or painful splenomegaly; one of the following symptomatic/progressive cytopenias: haemoglobin <10 g/dl, platelets <80 000/µl; neutrophils <1000/µl. Of note, AHA should be specifically treated.
Level of evidence V
Grade of recommendation: B

Survival outcomes from SEER database
N=227 patients treated with Splenectomy (68%) vs R (23%) vs R-chemo (9%)

"treatment only in the presence of symptomatic disease"
## SMZL: TREATMENT APPROACHES

### Table 4. Series of SMZL patients treated with rituximab-based approach

<table>
<thead>
<tr>
<th>Reference</th>
<th>Year</th>
<th>Study type</th>
<th>Scheme</th>
<th>Patient status</th>
<th>N</th>
<th>ORR</th>
<th>Duration</th>
<th>OS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Rituximab monotherapy</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bennett et al.</td>
<td>2005</td>
<td>Retrospective</td>
<td>R monotherapy</td>
<td>RR</td>
<td>11</td>
<td>91%</td>
<td>PFS 60% at 5 y</td>
<td>70% at 5 y</td>
</tr>
<tr>
<td>Tsimberidou et al.</td>
<td>2006</td>
<td>Retrospective</td>
<td>R monotherapy</td>
<td>First line</td>
<td>25</td>
<td>88%</td>
<td>FFS 86% at 3 y</td>
<td>95% at 3 y</td>
</tr>
<tr>
<td>Kalpadakis et al.</td>
<td>2007</td>
<td>Retrospective</td>
<td>R monotherapy</td>
<td>First line</td>
<td>16</td>
<td>100%</td>
<td>PFS 92% at 2.4 y</td>
<td>100% at 2.1 y</td>
</tr>
<tr>
<td>Else et al.</td>
<td>2012</td>
<td>Retrospective</td>
<td>R monotherapy</td>
<td>First line and RR</td>
<td>10</td>
<td>100%</td>
<td>DFS 89% at 3 y</td>
<td>NR</td>
</tr>
<tr>
<td>Kalpadakis et al.</td>
<td>2013</td>
<td>Retrospective</td>
<td>R monotherapy</td>
<td>First line</td>
<td>58</td>
<td>95%</td>
<td>PFS 73% at 5 y</td>
<td>92% at 5 y</td>
</tr>
<tr>
<td><strong>Rituximab + chemotherapy</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tsimberidou et al.</td>
<td>2006</td>
<td>Retrospective</td>
<td>R-chemo</td>
<td>First line</td>
<td>6</td>
<td>83%</td>
<td>FFS 100% at 3 y</td>
<td>100% at 3 y</td>
</tr>
<tr>
<td>Cervetti et al.</td>
<td>2010</td>
<td>Retrospective</td>
<td>R-2CDA</td>
<td>First line and RR</td>
<td>47*</td>
<td>87%</td>
<td>PFS 80% at 5 y</td>
<td>86% at 5 y</td>
</tr>
<tr>
<td>Else et al.</td>
<td>2012</td>
<td>Retrospective</td>
<td>R-chemo</td>
<td>First line and RR</td>
<td>33</td>
<td>100%</td>
<td>DFS 71% at 3 y</td>
<td>NR</td>
</tr>
<tr>
<td>Iannitto et al.</td>
<td>2015</td>
<td>Prospective</td>
<td>R-COMP</td>
<td>First line</td>
<td>51</td>
<td>84%</td>
<td>PFS 54% at 6 y</td>
<td>72% at 6 y</td>
</tr>
</tbody>
</table>

2CDA, 2-chlorodeoxyadenosine; chemotheraphy; DFS, disease-free survival; R, rituximab; RR, relapsed/refractory.

*Rituximab in 32 patients.

N=415

2. Used with permission of Elsevier Science & Technology Journals, from Extranodal Lymphomas, Peter G Isaacson and Andrew J Norton, 1994; permission conveyed through Copyright Clearance Center, Inc.

Peyer’s patch from terminal ileum composed of a cluster of B-cell follicles and related T-cell areas (T)^2
L, efferent lymphatics
## Distinct Mutation Profiles

In mucosa-associated lymphoid tissue (MALT) lymphoma of various sites

### Mutation frequency (%)

<table>
<thead>
<tr>
<th>Gene</th>
<th>Salivary gland (n=58)</th>
<th>Ocular adnexa (n=115)</th>
<th>Thyroid (n=13)</th>
<th>Stomach (n=36)</th>
<th>Lung (n=13)</th>
<th>Other (n=14)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TBL1XR1</td>
<td>24%</td>
<td>6%</td>
<td>8%</td>
<td>8%</td>
<td>8%</td>
<td>14%</td>
</tr>
<tr>
<td>GPR34</td>
<td>19%</td>
<td>1%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CCR6</td>
<td>5%</td>
<td>1%</td>
<td>8%</td>
<td>6%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PIK3CD</td>
<td>9%</td>
<td>3%</td>
<td>23%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TNFRSF14</td>
<td>3%</td>
<td>5%</td>
<td>46%</td>
<td>8%</td>
<td>8%</td>
<td></td>
</tr>
<tr>
<td>TET2</td>
<td>9%</td>
<td>4%</td>
<td>62%</td>
<td>8%</td>
<td>8%</td>
<td></td>
</tr>
<tr>
<td>NOTCH1</td>
<td>5%</td>
<td>2%</td>
<td>11%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TNFAIP3</td>
<td>3%</td>
<td>36%</td>
<td>8%</td>
<td>14%</td>
<td>8%</td>
<td></td>
</tr>
<tr>
<td>MYD88</td>
<td>2%</td>
<td>7%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>API2-MALT1</td>
<td>1%</td>
<td></td>
<td></td>
<td>28%</td>
<td>23%</td>
<td>7%</td>
</tr>
</tbody>
</table>

MARGINAL ZONE-LYMPHOMAS: CLINICAL DISTRIBUTION

"Homing":
MALT-Lymphoma: +++
Splenic MZL: + (KM, liver)
Nodal MZL: - (by exclusion!)

Courtesy of Medical University Vienna
140 PATIENTS

Gastric
n=61

Extragastric
n=79

\[ n=15 \]

- GI-tract: \( n=8 \)
- GI+non-GI: \( n=1 \)
- Non-GI: \( n=6 \)
- Bone-marrow: \( n=2 \)

\[ n=37 \]

- Stomach*: \( n=9 \)
- Bilateral non-GI \( n=8 \)
- “Other” \( n=20 \)
- Bone-marrow: \( n=1 \)

*Lung: \( n=4 \)

\[ P=0.045 \]

CLINICAL OUTCOMES ACCORDING TO MALT-IPI RISK GROUPS

PENTIXAFOR-PET/MR

Courtesy of Medical University Vienna
BONE MARROW INVOLVEMENT

Bone marrow involvement is not associated with the clinical outcomes of gastric mucosa-associated lymphoid tissue lymphoma

- Complete remission rate: **85.2%** (median follow-up 42 months (IQR, 23–66 months) and did not differ between the patients with and without BM involvement (78.6 and 85.7%; P = ns)
PET scan investigation may be considered when clinical and/or laboratory data suggest a transformation to high-grade histology or to guide the decision which lymph node should be biopsied [IV, B]

ESMO guidelines 2018

<table>
<thead>
<tr>
<th>Transformation:</th>
</tr>
</thead>
<tbody>
<tr>
<td>IELSG*:</td>
</tr>
<tr>
<td>157 MALT - 4%</td>
</tr>
<tr>
<td>85 SMZL - 5%</td>
</tr>
<tr>
<td>37 NMZL - 3%</td>
</tr>
<tr>
<td>Vienna:</td>
</tr>
<tr>
<td>327 MALT - 3.4%</td>
</tr>
<tr>
<td>(6.4 – 205 mos)</td>
</tr>
</tbody>
</table>
RISK OF TRANSFORMATION IN MALT-LYMPHOMA

Conclusion

- By PCR-based clonality analysis, we could prove a straight clonal relationship in 8/11 analysed cases of MALT lymphoma with HT
- Transformation occurred within the first 2.5 years after diagnosis in patients with clonal relationship, whereas time to aggressive lymphoma was longer in patients identified as clonally-unrelated
- Prognosis of transformed patients was poor except for patients with localised gastric transformation and no further extranodal disease

Arising either de novo or transforming from MALT-lymphoma

Decreasing incidence!!

Role of HP-eradication?

HELICOBACTER PYLORI ERADICATION THERAPY
Is effective in the treatment of early-stage H pylori–positive gastric diffuse large B-cell lymphomas

Table 2

| Clinicopathologic characteristic | Pure (de novo) DLBCL | DLBCL(MALT) | *P*
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>16</td>
<td>34</td>
<td></td>
</tr>
<tr>
<td>HPE rate, %</td>
<td>100 (16/16)</td>
<td>94.1 (32/34)</td>
<td>1.000†</td>
</tr>
<tr>
<td>pCR rate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All evaluable patients, %</td>
<td>68.8 (11/16)</td>
<td>52.9 (18/34)</td>
<td>0.365†</td>
</tr>
<tr>
<td>HP-eradicated patients</td>
<td>68.8 (11/16)</td>
<td>56.3 (18/32)</td>
<td>0.404†</td>
</tr>
<tr>
<td>HP-persistent patients</td>
<td>0 (0/0)</td>
<td>0 (0/2)</td>
<td></td>
</tr>
<tr>
<td>Depth of gastric wall involvement</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Submucosa or above, %</td>
<td>100 (5/5)</td>
<td>80 (8/10)</td>
<td>0.524†</td>
</tr>
<tr>
<td>Muscularis propria or beyond, %</td>
<td>54.5 (8/11)</td>
<td>29.4 (5/17)</td>
<td>0.248†</td>
</tr>
<tr>
<td>Time to pCR§</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (95% CI), mo</td>
<td>2.1 (0.6–3.7)</td>
<td>5.0 (2.8–7.5)</td>
<td>0.024†</td>
</tr>
<tr>
<td>Follow-up time of complete responders¶</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (95% CI), y</td>
<td>3.5 (0.7–6.3)</td>
<td>11.1 (7.8–14.4)</td>
<td></td>
</tr>
<tr>
<td>Relapse rate, %¶</td>
<td>0 (0/0)</td>
<td>0 (0/0)</td>
<td></td>
</tr>
</tbody>
</table>

### INFECTIONS AND MZL

**Helicobacter pylori:** stomach MZL  
**Borrelia burgdorferi:** cutaneous MZL (?), lymphoma of skin  
**Chlamydia psittaci:** ocular adnexa MZL  
**Campylobacter jejuni:** IPSID  
**Achromobacter Xylosoxidans:** BALT-Lymphoma  
**Hepatitis C:** splenic MZL, nodal MZL, MALT  
**Hepatitis B:** splenic MZL (?)  

---

**Table 1.** Comparison of clinical features of patients who underwent antiviral therapy as anti-lymphoma treatment with respect to those who did not.

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>%</th>
<th>Antiviral therapy as anti-lymphoma treatment</th>
<th>Test and P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes (134)</td>
<td>No (570)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male/female</td>
<td>57/77</td>
<td>43/57</td>
<td></td>
<td>$\chi^2 = 0.2, P = 0.698$</td>
</tr>
<tr>
<td>Age &gt;60 years</td>
<td>70/69</td>
<td>43/57</td>
<td></td>
<td>$\chi^2 = 21.5, P &lt; 0.001$</td>
</tr>
<tr>
<td>Histotypes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Follicular lymphoma</td>
<td>134</td>
<td>19%</td>
<td>12/9</td>
<td>$\chi^2 = 27.7, P &lt; 0.001$</td>
</tr>
<tr>
<td>MALT MZL</td>
<td>135</td>
<td>22%</td>
<td>29/22</td>
<td></td>
</tr>
<tr>
<td>Primary nodal MZL</td>
<td>59</td>
<td>8%</td>
<td>13/9</td>
<td></td>
</tr>
<tr>
<td>Splenic MZL</td>
<td>137</td>
<td>20%</td>
<td>36/27</td>
<td></td>
</tr>
<tr>
<td>Small lymphocytic lymphoma</td>
<td>37</td>
<td>5%</td>
<td>4/3</td>
<td></td>
</tr>
<tr>
<td>Lymphoplasmacytic lymphoma</td>
<td>53</td>
<td>8%</td>
<td>10/7</td>
<td></td>
</tr>
</tbody>
</table>

Counts (n) and percentage frequencies (%) with the Pearson’s $\chi^2$ test and the significance level (P-value) are reported.

MZL, marginal zone lymphoma; MALT, mucosa-associated lymphoid tissue; NOS, not otherwise specified; LDH, lactate dehydrogenase; UNL, upper normal limit.

---

**Vienna Series 1999 - 2017:**  
3 / 402 MALT lymphomas HCV + (0.7%)
## HP AND GASTRIC MALT

<table>
<thead>
<tr>
<th>AUTHOR</th>
<th>Year</th>
<th>Number</th>
<th>Response</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wotherspoon, et al</td>
<td>1993</td>
<td>6</td>
<td>5</td>
<td>83</td>
</tr>
<tr>
<td>Roggero, et al</td>
<td>1995</td>
<td>25</td>
<td>15</td>
<td>60</td>
</tr>
<tr>
<td>Bayerdörffer, et al</td>
<td>1995</td>
<td>33</td>
<td>23</td>
<td>70</td>
</tr>
<tr>
<td>Montalban, et al</td>
<td>1995</td>
<td>4</td>
<td>4</td>
<td>100</td>
</tr>
<tr>
<td>Savio, et al</td>
<td>1996</td>
<td>13</td>
<td>11</td>
<td>85</td>
</tr>
<tr>
<td>Neubauer, et al</td>
<td>1998</td>
<td>120</td>
<td>95</td>
<td>79</td>
</tr>
<tr>
<td>Steinbach, et al</td>
<td>1999</td>
<td>18</td>
<td>14</td>
<td>78</td>
</tr>
<tr>
<td>Nakamura, et al</td>
<td>2001</td>
<td>41</td>
<td>30</td>
<td>73</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td><strong>260</strong></td>
<td><strong>197</strong></td>
<td><strong>76</strong></td>
</tr>
</tbody>
</table>
### ASSESSMENT OF RESPONSE

**GELA histological grading system for post-treatment evaluation of gastric MALT lymphoma**

<table>
<thead>
<tr>
<th>Score</th>
<th>Lymphoid infiltrate</th>
<th>LEL</th>
<th>Stromal changes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete Histological remission (CR)</td>
<td>Absent or scattered plasma cells and small lymphoid cells in the LP</td>
<td>Absent</td>
<td>Normal or empty LP and/or fibrosis</td>
</tr>
<tr>
<td>Probable minimal residual disease (pMRD)</td>
<td>Aggregates of lymphoid cells or lymphoid nodules in the LP/MM and/or SM</td>
<td>Absent</td>
<td>Empty LP and/or fibrosis</td>
</tr>
<tr>
<td>Responding residual disease (rRD)</td>
<td>Dense, diffuse or nodular, extending around glands in the LP</td>
<td>Focal LEL or absent</td>
<td>Focal empty LP and/or fibrosis</td>
</tr>
<tr>
<td>No change (NC)</td>
<td>Dense diffuse or nodular</td>
<td>Present ‘may be absent’</td>
<td>No changes</td>
</tr>
</tbody>
</table>

MM, muscularis mucosa; LP, lamina propria; SM, submucosa; LEL, lymphoepithelial lesions.

Table reproduced from Gut, Copie-Bergman C, et al. 52, 1656, copyright 2003 with permission from BMJ Publishing Group Ltd. Images Courtesy of Medical University Vienna.
68GA-PENTIXAFOR PET/MR FOLLOW-UP

26 patients, HP-eradication
(46 post-eradication PET/MRs)

Comparison to matched biopsies (GELA)

Sensitivity: 95%
Specificity: 100%
The first-line treatment of all gastric MALT lymphomas is *H. pylori* eradication therapy independent of the stage. Nevertheless, the staging procedure has to be performed before starting eradication therapy.

**Patients who respond to eradication therapy (lymphoma regression) should not receive any other treatment**
Gastric MALT lymphoma stage I (n=108)

- **Hp eradication**
  - CR n=35 (32%)
  - Minimal residuals unchanged n=67 (62%)
  - PD n=6 (6%)

- **Minimal residuals Hp negative after 12 months**

---

Adapted from: Hancock BW, et al. Br J Haematol 2009;144(3):367–75. Reproduced under the terms of a the Creative Commons Deed, Attribution 2.5 Generic licence (CC BY 2.5; available at: https://creativecommons.org/licenses/by/2.5/#:~:text=Under%20the%20following%20terms%3A,endorses%20you%20or%20your%20use; accessed Jun 2022).
GASTRIC MALT LYMPHOMA: CR VS. PR AFTER INITIAL THERAPY

Median follow-up: 54 mos (23–100)

P=0.019
PROGRESSION OF DISEASE AT 24 MONTHS: POD24

Test set

Validation set
# MZL AND AUTOIMMUNE-DISEASES

## Table 1  Results

<table>
<thead>
<tr>
<th></th>
<th>Patients with AD</th>
<th>Patients without AD</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>61 (39%)</td>
<td>97 (61%)</td>
<td>—</td>
</tr>
<tr>
<td>Median age (months, IQR)</td>
<td>56 (48–69)</td>
<td>67 (54–76)</td>
<td>0.0004</td>
</tr>
<tr>
<td>Extragastic disease</td>
<td>45/61 (74%)</td>
<td>52/97 (54%)</td>
<td>0.012</td>
</tr>
<tr>
<td>Monoclonal gammopathy</td>
<td>14/41 (34%)</td>
<td>22/45 (49%)</td>
<td>0.194</td>
</tr>
<tr>
<td>Trisomy 3</td>
<td>8/49 (16%)</td>
<td>17/50 (34%)</td>
<td>0.043</td>
</tr>
<tr>
<td>Trisomy 18</td>
<td>5/49 (10%)</td>
<td>4/50 (8%)</td>
<td>0.703</td>
</tr>
<tr>
<td>t(11;18)</td>
<td>9/49 (18%)</td>
<td>17/50 (34%)</td>
<td>0.077</td>
</tr>
<tr>
<td>t(14;18)</td>
<td>4/49 (8%)</td>
<td>6/50 (12%)</td>
<td>0.548</td>
</tr>
<tr>
<td>t(1;14)</td>
<td>0/49 (0%)</td>
<td>0/50 (0%)</td>
<td>—</td>
</tr>
<tr>
<td>t(3;14)</td>
<td>1/49 (2%)</td>
<td>1/50 (2%)</td>
<td>—</td>
</tr>
<tr>
<td>Plasmacellular differentiation</td>
<td>19/54 (35%)</td>
<td>21/80 (26%)</td>
<td>0.336</td>
</tr>
<tr>
<td>Median time to relapse (months, IQR)</td>
<td>71 (43–131)</td>
<td>307 (40–307)</td>
<td>0.354</td>
</tr>
<tr>
<td>Autoantibodies</td>
<td>43/52 (83%)</td>
<td>13/42 (31%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Multifocal disease</td>
<td>31/60 (52%)</td>
<td>35 /98 (36%)</td>
<td>0.069</td>
</tr>
<tr>
<td>Relapse</td>
<td>21/52 (40%)</td>
<td>21/63 (33%)</td>
<td>0.445</td>
</tr>
</tbody>
</table>

**Abbreviation:** IQR, inter-quartile-range. Bold signifies statistically significant.

**Response to HP–eradication worse in AD!!**
99/116 (85%) complete HP-Status
34% HP-negative (incl histology, breath test and serology)

Possible reasons:
- “Blind-Eradication”
- Referral Bias

WHO 2008 → 5–10% HP-negative patients!

1999-2004
N = 9 (26%)
9/49 = 18%
p=0.02

2004-2015
N = 25 (74%)
25/50 = 50%
EFFICACY OF ERADICATION THERAPY

In Helicobacter pylori-negative gastric mucosa-associated lymphoid tissue lymphoma: A meta-analysis

Background and Aims: The role of eradication therapy in Helicobacter pylori-negative gastric mucosa-associated lymphoid tissue (MALT) lymphoma remains controversial. The aim of this study was to investigate the efficacy of H. pylori eradication therapy as a first-line treatment for H. pylori-negative gastric MALT lymphoma.

Methods: A literature search of studies published until October 2019 was performed using electronic databases. Studies that reported treatment response to eradication therapy as an initial treatment for patients with H. pylori-negative gastric MALT lymphoma were eligible for inclusion. The primary outcome was the complete remission rate after eradication therapy.

Results: Twenty-five studies were included in the analyses. The overall pooled complete remission rate was 29.3% (95% confidence interval [CI], 22.2%–37.4%, $I^2 = 41.5$%). There was no publication bias, and the sensitivity analyses showed consistent results. The pooled complete remission rates were lower in the subgroups of studies that had a higher incidence of translocation t(11;18)(q21;q21) (19.9%, 95% CI, 11.6%–32.0%), studies that used serological tests to exclude H. pylori infection (27.5%, 95% CI, 20.1%–36.4%), and studies where non-response to eradication therapy was determined at <12 months after treatment (27.0%, 95% CI, 15.5%–42.7%). Meta-regression analysis revealed that the pooled estimate was not significantly different in terms of the characteristics of individual studies.

Conclusions: Although the complete remission rate after eradication therapy is not high, it can be used as an initial treatment option in a subset of patients with H. pylori-negative gastric MALT lymphoma. Further studies to identify subgroups of patients who may benefit from eradication therapy are needed.
IN Volvement of non-HeliCobacter Pylori Helicobacter infections

In $H$. pylori-negative gastric MALT lymphoma pathogenesis and efficacy of eradication therapy

<table>
<thead>
<tr>
<th>Target gene</th>
<th>Target species</th>
<th>Primer sequences (F: forward, R: reverse)</th>
<th>Annealing temperature (°C)</th>
<th>Cycle number</th>
<th>Fragment size (bp)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ureA</td>
<td>$H$. suis</td>
<td>F: CACCACCCGGGGAAGTGATCTTG R: CTACATCAATCAAATGCACCGGTTTTTCTTCG</td>
<td>60</td>
<td>40</td>
<td>253</td>
</tr>
<tr>
<td>ureA</td>
<td>$H$. bizzozeronii</td>
<td>F: CGCTTTGAACCCCGTGAGAAAA R: TATCGCAGGCAATTCAACAACA</td>
<td>60</td>
<td>40</td>
<td>172</td>
</tr>
<tr>
<td>ureB</td>
<td>$H$. felis</td>
<td>F: TCCCACTACCGGGATCGTG R: CAGCGTTTACAATCAAGGCCCCTCA</td>
<td>60</td>
<td>50</td>
<td>350</td>
</tr>
<tr>
<td>ureAB</td>
<td>$H$. salomonis</td>
<td>F: CTTTGGGTCTGTGCGCTGCTGTGCGCTG R: CATCGCAGGATAGTTACCGCCTCA</td>
<td>62</td>
<td>40</td>
<td>219</td>
</tr>
<tr>
<td>ureA</td>
<td>$H$. heilmannii s.s</td>
<td>F: CTTTCTCTGGTGAATGATTCTC R: CAGGGTGATTGCAAGGAG</td>
<td>60</td>
<td>40</td>
<td>368</td>
</tr>
</tbody>
</table>

**Results** The API2-MALT1 mutation was observed in 13/182 patients (7.1%), none of whom were cured by eradication therapy. Helicobacter pylori-negative cases had a significantly higher non-Helicobacter pylori helicobacter infection rate than Helicobacter pylori-positive cases (16/29, 55% vs. 3/29, 10%; $P<0.05$). Among the Helicobacter pylori-negative cases, non-Helicobacter pylori helicobacter-positive cases had a significantly higher complete response rate than non-Helicobacter pylori helicobacter-negative cases (12/16, 75% vs. 3/13, 23%; $P<0.05$).

**Conclusion** Helicobacter pylori-negative and API2-MALT1-negative gastric MALT lymphoma cases exhibited a high rate of non-Helicobacter pylori helicobacter infections, which may have contributed to the success of eradication therapy. Therefore, we recommend eradication therapy as a first-line treatment for non-Helicobacter pylori helicobacter-positive gastric MALT lymphoma.

and probably resulting in a publication bias toward positive cases. Based on these results, antibiotic therapy using doxycycline appears to be a reasonable first-line therapy for patients with OAML. Antibiotics, however, remain experimental for the time being in patients with other non-GI MALT lymphomas. Further preclinical studies as well as large-scale therapeutic trials are warranted to define the role of antibiotic therapy in such patients. (Blood. 2013;122(8):1350-1357)
### BEYOND ANTIBIOTICS... ?

<table>
<thead>
<tr>
<th>Localized disease:</th>
<th>Radiotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Systemic treatment</td>
</tr>
<tr>
<td></td>
<td>Radio-immunotherapy (RIT)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Disseminated disease:</th>
<th>Systemic treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Radio-immunotherapy (RIT)</td>
</tr>
</tbody>
</table>

### Recommendation
Both radiotherapy and chemotherapy have a curative potential in localised gastric MALT lymphoma. There is no recommendation in favour of one of these two modalities. If clinical trials are available, patients should be included.
LONG-TERM OUTCOME OF 487 PATIENTS WITH EARLY-STAGE EXTRA-NODAL MARGINAL ZONE LYMPHOMA

Characteristics of early stage patients

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N=487</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (range)</td>
<td>60 (9-92)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>277 (57%)</td>
</tr>
<tr>
<td>Male</td>
<td>210 (43%)</td>
</tr>
<tr>
<td>Stage</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>434 (89%)</td>
</tr>
<tr>
<td>II</td>
<td>53 (11%)</td>
</tr>
<tr>
<td>Primary site at diagnosis</td>
<td></td>
</tr>
<tr>
<td>Stomach</td>
<td>155 (32%)</td>
</tr>
<tr>
<td>Orbit</td>
<td>68 (14%)</td>
</tr>
<tr>
<td>Lung</td>
<td>60 (12%)</td>
</tr>
<tr>
<td>Skin</td>
<td>61 (13%)</td>
</tr>
<tr>
<td>Head and neck</td>
<td>26 (5%)</td>
</tr>
<tr>
<td>Thyroid</td>
<td>9 (2%)</td>
</tr>
<tr>
<td>Other</td>
<td>108 (22%)</td>
</tr>
</tbody>
</table>

Cumulative incidence of relapse/progression

Cumulative incidence of relapse by primary disease site

Overall survival

N=487 (72 Deaths)
Median survival: 15 years, 95%CI (14.4-Not achieved)
Median follow-up for survivors: 5 years

Teckie S, et al. Ann Oncol 2017;28:1064–9. © 2017 European Society for Medical Oncology. Published by Elsevier Ltd. All rights reserved.
4 Gy vs 24 Gy radiotherapy for follicular and marginal zone lymphoma (FoRT)

Long-term follow-up of a multicentre, randomised, phase 3, non-inferiority trial

Added value of this study
The results of this trial confirm that, with long-term follow-up, 4 Gy in two fractions is not non-inferior to 24 Gy in 12 fractions for local control when treating follicular lymphoma, in both the radical and palliative setting. Exploratory analyses show the same effect for marginal zone lymphoma and orbital lymphoma.

Implications of all the available evidence
In the palliative setting, 4 Gy of radiotherapy might provide a pragmatic treatment for local symptom control, but, for durable local control of follicular and marginal zone lymphoma, 24 Gy should be used.
Relapses total: 58 / 172 (39%)
Median time to relapse: 60 months (range: 3–307)
90Y–IBRITUMOMAB TIUXETAN (ZEVALIN)


<table>
<thead>
<tr>
<th>Author</th>
<th>Setting</th>
<th>Pts</th>
<th>ORR%</th>
<th>CR%</th>
<th>PFS</th>
<th>Toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Esmaeli</td>
<td>OAL de novo</td>
<td>9</td>
<td>89%</td>
<td>78%</td>
<td>-</td>
<td>Thrombocytopenia, Anemia</td>
</tr>
<tr>
<td>Hoffmann</td>
<td>MALT relapsed</td>
<td>6</td>
<td>83%</td>
<td>67%</td>
<td>-</td>
<td>Neutropenia, Thrombocytopenia</td>
</tr>
<tr>
<td>Vanazzi</td>
<td>MALT relapsed</td>
<td>30</td>
<td>90%</td>
<td>77%</td>
<td>N.R.</td>
<td>Neutropenia, Thrombocytopenia</td>
</tr>
<tr>
<td>Lossos</td>
<td>MALT de novo</td>
<td>11</td>
<td>16%</td>
<td>88%</td>
<td>47.6</td>
<td>Neutropenia, Thrombocytopenia</td>
</tr>
<tr>
<td>Samniego</td>
<td>MZL de novo</td>
<td>11</td>
<td>100%</td>
<td>-</td>
<td>81.8</td>
<td>Neutropenia, Thrombocytopenia</td>
</tr>
</tbody>
</table>

Median follow-up 5.3 y

Haematological toxicity after RIT

<table>
<thead>
<tr>
<th>Haematological adverse event</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anaemia</td>
<td>13</td>
<td>2</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>7</td>
<td>4</td>
<td>5</td>
<td>9</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>3</td>
<td>8</td>
<td>7</td>
<td>11</td>
</tr>
</tbody>
</table>

- 2 patients relapsed after CR (7%)
- 18/23 in remission after >3 years
- 12 after >5 years
## Ofatumumab (O-MA1 trial):

RR: 81%  
CR: 50%  
F/U: 25.1 mos, 1 relapse

### Investigator Study Design Patients, N (M/F) Median age, y (Range) Stage Treatment Route ORR (%) Detailed response ORR G vs. EG Treatment failure Median f/u, mo (Range)

**Conconi, et al. 2003**  
Phase II  
35 (11/24)  
15 (43%)/20 (57%)  
57 (27–85)  
I-IVE  
R375 mg/m² q7x4  
i.v.  
73  
CR, 15 (44%); PR, 10 (29%); SD, 6 (18%); PD, 3 (9%)  
64% vs. 80%  
9/25 (36%) of responding patients relapsed at median of 14 mo  
15 (1–23)

**Martinelli, et al. 2005**  
Phase II  
27 (15/12)  
G  
53 (32–80)  
I-IVE  
R375 mg/m² q7x4  
i.v.  
77  
CR, 12 (46%); PR, 8 (31%); SD, 6 (23%); NE, 1  
NA  
2/20 (10%) of responding patients relapsed at median of 14 and 26 mo  
33

**Lossos, et al. 2007**  
Phase II  
12 (5/7)  
3 (25%)/9 (75%)  
55 (34–79)  
I-IVE  
R375 mg/m² q7x4  
i.v.  
67  
CR, 2 (17%); PR, 6 (50%); SD, 3 (25%); PD, 1 (8%)  
67% vs. 70%  
6/8 (75%) of responding patients relapsed at median of 5 mo  
20 (6–53)

**Raderer, et al. 2003**  
Retrospective  
9 (5/4)  
3 (67%)/3 (33%)  
ND  
II-IVE  
R375 mg/m² q7x4  
i.v.  
56  
CR, 3 (33%); PR, 2 (22%); SD, 4 (44%)  
ND  
1/5 (20%) of responding patients relapsed at 15 mo  
10–27

**Ferreri, et al. 2005**  
Retrospective  
8 (1/7)  
Orbital  
56 (22–74)  
I-IVE  
R375 mg/m² q7x4  
i.v.  
63  
CR, 3 (38%); PR, 2 (25%); SD, 1 (16%); PD, 2 (25%)  
NA  
5/5 (100%) of responding patients relapsed at 7 and 11 mo  
62

**Morales, et al. 2008**  
Retrospective  
5 (2/3)  
Skin  
64 (38–75)  
R375 mg/m² q7x4 (1 pt received maintenance therapy)  
i.v.  
60  
CR, 1 (20%); PR, 3 (40%); SD, 1 (20%); PD, 1 (20%)  
NA  
1/3 (33%) of responding patients relapsed at 21 mo  
27 (3–94)

**Valencak, et al. 2008**  
Retrospective  
5 (4/1)  
Skin  
51 (37–68)  
R375 mg/m² q7x4  
i.v.  
100  
CR, 4 (80%); PR, 1 (20%)  
NA  
2/5 (40%) relapsed at 21 mo  
48 (10–75)
ANTI-CD20: INFLUENCE ON HISTOLOGY?

Plasmacytic differentiation:
N=21 (19 gastric, 2 colonic)

PCD before R: 2 / 21 (9%)
PCD following R: 7 / 19 (37%)
## SELECTED CHEMOTHERAPY STUDIES

<table>
<thead>
<tr>
<th>FIRST AUTHOR</th>
<th>STUDY DESIGN</th>
<th>NO. OF PATIENTS</th>
<th>GASTRIC/EXTRAGASTRIC, %</th>
<th>STAGE</th>
<th>THERAPY</th>
<th>RESPONSE RATE, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hammel 1995</td>
<td>Retrospective</td>
<td>24</td>
<td>Gastric</td>
<td>I, IVE</td>
<td>Alkylating agents (po) continuously for 12-24 mo (cyclophosphamide 100 mg/m² or chlorambucil)</td>
<td>ORR, 100 (CRR, 75)</td>
</tr>
<tr>
<td>Zucca 2013</td>
<td>Randomized</td>
<td>231</td>
<td>37/63</td>
<td>I-IVE</td>
<td>Chlorambucil (po) vs R-chlorambucil (chlorambucil 6 mg/m² daily d1-42 in a 4-wk cycle × 4 followed by d1-14 in a 4-wk cycle × 4; R 375 mg/m² d1, 8, 15, and 22, then every 4 wk in absence of progression)</td>
<td>ORR, 87 vs 94 (CRR, 65 vs 78)</td>
</tr>
<tr>
<td>Hancock 2009</td>
<td>Randomized</td>
<td>110</td>
<td>Gastric</td>
<td>I, IIE</td>
<td>Chlorambucil (po) vs observation after HP eradication (chlorambucil maintenance: 6 mg/m² daily d1-14 in a 4-wk cycle × 6 after successful HP eradication)</td>
<td>5-Y recurrence rate, 21 vs 11 (P = 0.15, NS)</td>
</tr>
<tr>
<td>Lévy 2013</td>
<td>Retrospective</td>
<td>49</td>
<td>Gastric</td>
<td>I-VE</td>
<td>R-chlorambucil vs R-monotherapy (R 375 mg/m² d1, 8, 15, and 22, then every 4 wk; chlorambucil 6 mg/m² daily d1-42 followed by d1-14 in a 4-wk cycle for 4 mo)</td>
<td>ORR, 93 vs 81</td>
</tr>
<tr>
<td>Salar 2014</td>
<td>Phase 2</td>
<td>60</td>
<td>33/66</td>
<td>I-VE</td>
<td>R-bendamustine (R 375 mg/m² d1; bendamustine 90 mg/m² d1 + 2 in a 4-wk cycle × 4 q6, depending on response)</td>
<td>ORR, 100 (CRR, 98)</td>
</tr>
<tr>
<td>Kiesewetter 2013</td>
<td>Retrospective</td>
<td>14</td>
<td>Extragastric</td>
<td>I-VE</td>
<td>R-bendamustine (R 375 mg/m² d1; bendamustine 90 mg/m² d1 + 2 in a 3-wk cycle × 6)</td>
<td>ORR, 92 (CRR, 71)</td>
</tr>
<tr>
<td>Raderer 2006</td>
<td>Retrospective</td>
<td>26</td>
<td>27/73</td>
<td>I-VE</td>
<td>R-CHOP/R-CNOP (R 375 mg/m² d1; cyclophosphamide 750 mg/m² d2, doxorubicin 50 mg/m² d2 or mitoxantrone 8 mg/m² d2, vincristine 1.4 mg/m², prednisone d1-5 every 3 wk × 6-8)</td>
<td>ORR, 100 (CRR, 77)</td>
</tr>
<tr>
<td>Jäger 2003</td>
<td>Phase 2</td>
<td>26</td>
<td>73/37</td>
<td>I-VE</td>
<td>Cisplatin (iv) (0.12 mg/kg d1-5 every 4 wk × 6)</td>
<td>ORR, 100 (CRR, 84)</td>
</tr>
<tr>
<td>Troch 2013</td>
<td>Phase 2</td>
<td>40</td>
<td>53/48</td>
<td>I-VE</td>
<td>R-cisplatin (iv) (R 375 mg/m² d1; cisplatin 1.0 mg/kg d1-4 every 3 wk × 6)</td>
<td>ORR, 81 (CRR, 58)</td>
</tr>
<tr>
<td>Zinzani 2004</td>
<td>Phase 2</td>
<td>31</td>
<td>Extragastric</td>
<td>IE</td>
<td>FM or CVP (iv) (fludarabine 25 mg/m² d1-3 and mitoxantrone 10 mg/m² d1-3) or cyclophosphamide 400 mg/m² d1-5, vincristine 1.4 mg/m² d1, and prednisone every 3 wk × 6)</td>
<td>ORR, 100 (CRR, 100)</td>
</tr>
<tr>
<td>Salar 2009</td>
<td>Phase 2</td>
<td>22</td>
<td>55/46</td>
<td>I-VE</td>
<td>R-fludarabine (iv, po; R 375 mg/m² d1; fludarabine 25 mg/m² iv or 40 mg po d1-5 every 4 wk × 6-8)</td>
<td>ORR, 100 (CRR, 90)</td>
</tr>
</tbody>
</table>

CRR indicates complete remission rate; CVP, cyclophosphamide, vincristine, and prednisone; FM, fludarabine and mitoxantrone; HP, Helicobacter pylori; iv, intravenously; NS, nonsignificant; ORR, overall response rate; po, orally; R, rituximab; R-CHOP/CNOP, rituximab, cyclophosphamide, doxorubicin/mitoxantrone, vincristine, and prednisone; sc, subcutaneously.

UP-FRONT CHEMO-BASED TREATMENT OF MALT LYMPHOMA

IELSG 19 Chlorambucil +/- R¹,²

- Randomised Phase III, 454 patients
- Chlorambucil 5-year EFS 51%
- Rituximab 5-year EFS 50%
- R-Chlorambucil 5-year EFS 68%

MALT 2008-01 R-Bendamustine³,⁴

- Phase II, 60 patients
- ORR 100%, CRu 98%
- EFS 7yr 88%
- Option for treatment stop - CR4 (75%)

---

CHEMO-FREE APPROACHES: RITUXIMAB/LENALIDOMIDE (R2)


Overall response rate 80.4% (37/46)
- Complete remission 54.3% (25/46)
- Partial remission 26.1% (12/46)
- Stable disease 17.4% (8/46)
- Progressive disease 2.3% (1/46)

Number of patients 46
- Median FUP: 38.6 months
- Median PFS: Not reached
- Number of relapses 7 (11–34 m)
- Alive at last FUP: 94% (32/34)
- Disease related deaths 1 (transformed)
Some patients further improved 44+ months after Thal / Len.

Median time to best response 7.3 months.
DELAYED EFFICACY AFTER TREATMENT WITH LENALIDOMIDE OR THALIDOMIDE
In patients with mucosa-associated lymphoid tissue lymphoma

Retrospective analysis of 25 patients treated with lenalidomide (=18) or thalidomide (=7)
Thalidomide did not result in objective responses in the initially published results of a pilot trial … BUT …
28% of patients experienced delayed onset response (thalidomide n=2, lenalidomide n=5)
Four patients improved to a better outcome according to RECIST/ GELA (PR → CR, SD → CR, PD → CR, SD → PR)
Also, the combination of R-LEN resulted in late onset remissions (AGMT MALT2, Blood 2016)

Late remissions – a common phenomenon in MALT lymphoma?

AUGMENT: RITUXIMAB + LENALIDOMIDE (R²) VS RITUXIMAB + PLACEBO – PRIMARY EFFICACY RESULTS

At a median follow-up of 28.3 mo, the primary endpoint of superior PFS was met for R² over R-placebo (median PFS: 39.4 vs 14.1 mo, respectively; P<0.0001)

ORR and CR were significantly improved for R² (78% vs 53% and 34% versus 18%)

Status quo: FDA approved in FL and MZL, EMA approved for r/r FL

AUGMENT SUBGROUP – R² IN R/R MZL PATIENTS

After a median follow-up of 27.9 months (range, 0.5–51.3), median PFS was 20.2 months in the R² arm vs 25.2 months in the R-placebo arm (P=1.0)
# CHEMO-FREE TREATMENT FOR MALT LYMPHOMA

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Author</th>
<th>Design</th>
<th>N (Gastric)</th>
<th>ORR</th>
<th>CRR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rituximab</td>
<td>Conconi 2003</td>
<td>Phase II</td>
<td>35 (43%)</td>
<td>73%</td>
<td></td>
</tr>
<tr>
<td>Rituximab</td>
<td>Martinelli 2005</td>
<td></td>
<td>77%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ofatumumab</td>
<td>Kiesewetter, Raderer</td>
<td></td>
<td>81%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bortezomib</td>
<td>Troch 2009</td>
<td></td>
<td>81%</td>
<td>44%</td>
<td></td>
</tr>
<tr>
<td>Bortezomib</td>
<td>Conconi 2010</td>
<td></td>
<td>48%</td>
<td>31%</td>
<td></td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>Ferreri 2016</td>
<td></td>
<td>53%</td>
<td>26%</td>
<td></td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>Ferreri 2017</td>
<td></td>
<td>47%</td>
<td>23%</td>
<td></td>
</tr>
<tr>
<td>Azithromycin</td>
<td>Lagler, Raderer</td>
<td></td>
<td>25%</td>
<td>13%</td>
<td></td>
</tr>
<tr>
<td>Lenalidomide</td>
<td>Kiesewetter, Raderer</td>
<td></td>
<td>61%</td>
<td>33%</td>
<td></td>
</tr>
<tr>
<td>R-Lenalidomide</td>
<td>Kiesewetter, Raderer</td>
<td></td>
<td>80%</td>
<td>54%</td>
<td></td>
</tr>
</tbody>
</table>

IELSG-19 5-year EFS 50% (n=138)\(^1\)

R-Mono 375 mg/m\(^2\) 4 x weekly

"very elegant approach"- combine antibiotic and immunomod. Aspects!

No long-term data?

---

**IBRUTINIB**

- **N=63 (MALT 32, nodal 17, splenic 14)**
  - Events: 13 PD, 7 relapse after initial response and 6 PDs after SD
  - No cases of HGT
  - Failures involved the primary site of disease in all cases but two

---

**Clarithromycin**

- **N = 55**
  - ORR 54%, 24% CR
  - 52% PFS 36 months

---

CHEMO VS IMMUNOTHERAPY

ORR:
90% vs 68%

CR:
75% vs 73%

Kiesewetter B, et al. Cancers 2020, 12(12), 3533, available at: https://www.mdpi.com/2072-6694/12/12/3533/htm. Reproduced under the terms of the Creative Commons Attribution-NonCommercial-No Derivatives License (CC BY NC ND; available at: https://creativecommons.org/licenses/by-nc-nd/4.0/; accessed April 2022).
Doxycyclin
Clarithromycin
Radiotherapy
Surgery
Wait and see
Local therapy
Immunotherapy
Chemo +/- Antibody
Other antibiotics
Anti CD20
Immunomodulatory

...“a distinctive type of B-cell lymphoma arising from mucosa-associated lymphoid tissues in the gastrointestinal tract”…
HP-eradication is standard for gastric MALT lymphoma

OAML may also be treated with antibiotics upfront

Both radiotherapy and systemic therapy may be applied in localised disease

The optimal systemic standard remains to be defined:
- Chemo (+ antibody) for quick remissions
- Immunotherapy in patients with indolent disease
THANK YOU!