



FL

## Vitamin D insufficiency is predictive of early clinical failure as well as inferior longer-term prognosis in patients with grade 1–3a Follicular Lymphoma

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On 25<sup>th</sup> August 2017, in the [Blood Cancer Journal](#), [S.I. Tracy](#) from the [Mayo Clinic](#), Rochester, MN, USA, and colleagues [published](#) findings from their observational prospective cohort study exploring whether Vitamin D Insufficiency (VDI; 25(OH)D <20ng/ml) is associated with poorer outcomes in patients with Follicular Lymphoma (FL).

Between 2002 and 2012, 920 FL grade 1–3a patients were enrolled in the Molecular Epidemiology Resource of the University of Iowa/Mayo Clinic Lymphoma Specialized Program of Research Excellence. Of these, 278 did not have serum samples taken within 120 days of diagnosis and so were excluded from the analysis.

### Key Highlights:

#### Patients

- Median age at diagnosis = 60 years (range, 23–93)
- Initial therapy:
  - R-CHOP = 118; R-CVP = 85; BR = 45; rituximab monotherapy = 76; other therapies = 96; observation = 218

#### Vitamin D levels

- Overall median serum 25(OH)D level = 29ng/ml (SD 11.9ng/ml)
- Median vitamin D levels were similar across treatment groups
- Using a threshold of <20ng/ml, prevalence of VDI:
  - Overall = 19% (120/642)
  - Pts treated with Immunochemotherapy (IC) = 23% (58/252)
  - Pts who underwent observation = 17% (36/218)
  - Pts treated with rituximab monotherapy = 14% (11/76)
  - Pts treated with other therapies = 16% (15/96)
- VDI was associated with non-white race ( $P = 0.03$ ), obesity ( $P = 0.001$ ), and lower performance status ( $P = 0.001$ ); these associations also persisted within some specific treatment groups

#### Outcomes

- Median follow-up = 59 months (range, 1–144)
- Event reported in 297 patients (46%); death reported in 78 patients (12%), lymphoma-related death reported in 42 patients (6.5%)
- EFS12 = 84% (95% CI, 82–87%)
- VDI was associated with inferior:
  - In all pts: EFS12 (OR = 2.05; 95% CI, 1.18–3.54), OS (HR = 2.35; 95% CI, 1.37–4.02), and LSS (HR = 2.97; 95% CI, 1.52–5.80)
  - In IC pts: EFS12 (OR = 3.00; 95% CI, 1.26–7.13), OS (HR = 2.86; 95% CI, 1.39–5.85), and LSS (HR = 2.96; 95% CI, 1.29–6.79)
  - In observed pts: OS (HR = 2.85; 95% CI, 1.20–6.76)
  - In other therapy pts: OS (HR = 3.06; 95% CI, 1.01–9.24)
  - In pts treated with any rituximab containing therapy: EFS12 (OR = 2.40; 95% CI, 1.12–5.14), OS (HR = 2.99; 95% CI, 1.50–5.97), and LSS (HR = 3.48; 95% CI, 1.55–7.83)

Overall, the group concluded that VDI is predictive of early clinical failure as well as inferior longer-term prognosis in patients with FL. The authors go on to say that their data supports the inclusion of serum 25(OH)D measurement at diagnosis into routine studies in order to identify patients who are at risk of early clinical failure. Lastly, the group conclude future studies should explore if outcomes based on supplementation with vitamin D can improve outcomes of FL patients.

#### Abstract:

We evaluated whether vitamin D insufficiency (VDI; 25(OH)D <20 ng/ml) was associated with adverse outcomes among follicular lymphoma (FL) patients using an observational prospective cohort study of 642 FL patients enrolled from 2002-2012. The median age at diagnosis was 60 years. At a median follow-up of 59 months, 297 patients (46%) had an event (progression, treatment failure), 78 had died and 42 (6.5%) had a lymphoma-related death. VDI was associated with inferior event-free survival (EFS) at 12 months (EFS12, odds ratio (OR)=2.05; 95% confidence interval (CI) 1.18-3.54), overall survival (OS, hazards ratio (HR)=2.35; 95%CI 1.37-4.02), and lymphoma-specific survival (LSS, HR=2.97; 95% CI 1.52-5.80) for the full cohort. Among patients treated with immunochemotherapy (IC), VDI was associated with inferior EFS12 (OR=3.00; 95% CI 1.26-7.13), OS (HR=2.86; 95% CI 1.39-5.85), and LSS (HR=2.96; 95% CI 1.29-6.79). For observed patients, VDI was associated with inferior OS (HR=2.85; 95% CI 1.20-6.76). For other therapies, VDI was associated with inferior OS (HR=3.06; 95% CI 1.01-9.24). Our work is the first to reveal an association of VDI with early clinical failure, and to demonstrate an association of VDI with adverse outcomes among patients who are observed or treated with therapies other than IC. Our findings suggest a potentially modifiable prognostic factor to address in patients with FL.

#### References

1. Tracey S.L. *et al.* Vitamin D insufficiency is associated with an increased risk of early clinical failure in follicular lymphoma. *Blood Cancer Journal*. 2017 Aug 25;7(8):e595. DOI: [10.1038/bcj.2017.70](https://doi.org/10.1038/bcj.2017.70).