Supplements to EssCD guideline

Supplement 1: GRADE system

GRADE system: Step 1, grade the evidence

A= high quality evidence; B= moderate quality evidence; C= poor quality evidence
If RCTs, start by assuming high quality (grade A), but then grade down for:
- Serious methodologic limitations
- Indirectness in population, intervention, or outcome
- Inconsistent results
-Imprecision in estimates
- High likelihood of publication bias

If no RCTs, start by assuming low quality (grade C), but then grade up for:
- Large, or very large treatment effects
- All plausible biases that would diminish the effect of the intervention
- Dose-response gradient

GRADE system: Step 2, grade the recommendation

1= strong recommendation
2= weak recommendation

	Clarity of risk/benefit	Quality of supporting evidence	Implications
1A. Strong recommendation. High quality evidence.	Benefits clearly outweigh risk and burdens, or vice versa.	Consistent evidence from well-performed RCTs or overwhelming evidence in some other form. Further research is unlikely to change our confidence in estimating benefit and risk.	Strong recommendation, can apply to most patients in most circumstances without reservation.
1B. Strong recommendation. Moderate quality evidence.	Benefits clearly outweigh risk and burdens, or vice versa.	Evidence from RCTs with important limitations (inconsistent results, methodological flaws, indirect or imprecise), or very strong evidence in some other form. Further research (if performed) is likely to have an impact on our confidence in estimating benefit and risk and may change the estimate.	Strong recommendation, likely to apply to most patients.
1C. Strong recommendation. Low quality evidence.	Benefits appear to outweigh risk and burdens, or vice versa.	Evidence from observational studies, unsystematic clinical experience, or from RCTs with serious flaws. Any estimate of effect is uncertain.	Relatively strong recommendation; might change when higher quality evidence becomes available.
2A. Weak recommendation. High quality evidence.	Benefits closely balanced with risks and burdens	Consistent evidence from well performed RCTs or overwhelming evidence in some other form. Further research is unlikely to change our confidence in the estimate of benefit and risk.	Weak recommendation, best action may differ depending on circumstances or patients or social values.
2B. Weak recommendation. Moderate quality evidence.	Benefits closely balanced with risks and burdens, some uncertainly in the estimates of benefits, risks and burdens	Evidence from randomized, controlled trials with important limitations (inconsistent results, methodological flaws, indirect or imprecise), or very strong evidence in some other form. Further research (if performed) is likely to have an impact on our confidence in estimating benefit and risk and may change the estimate.	Weak recommendation, alternative approaches likely to be better for some patients under some circumstances.
2C. Weak recommendation. Low quality evidence.	Uncertainty in the estimates of benefits, risks, and burdens; benefits may be closely balanced with risks and burdens.	Evidence from observational studies, unsystematic clinical experience, or from RCTs with serious flaws. Any estimate of effect is uncertain.	Very weak recommendation; other alternatives may be equally reasonable.

Table S1: Narratives detailing the evidence and grade of recommendations

Supplement 2:

List of Abbreviations

AGA anti Gliadin antibodies

BMI Body Mass Index

CD Coeliac disease

2-CDA Cladribine (2-chloro-2'-deoxyadenosine)

CVID Common Variable Immune Deficiency

DBE Double balloon enteroscopy

DEXA Dual-energy X-ray absorptiometry

DGP Deamidated Gliadin Antibodies

DH Dermatitis herpetiformis

DIF Direct immunofluorescence

EATL Enteropathy associated T-cell lymphoma

ELISPOT Enzyme-linked immunospot

EMA Endomysium antibodies

ESPGHAN European Society for Paediatric Gastroenterology, Hepatology, and Nutrition

GA Gluten ataxia

GFD Gluten Free Diet

GI Gastrointestinal

GIPs Gluten Immunogenic Peptides

GWAS Genome-wide association studies

HLA Human Leucocyte Antigen

IBD Inflammatory Bowel disease

IBS Irritable Bowel syndrome

IELs Intraepithelial lymphocytes

IL Interleukin

INF Interferon

6MMP 6-methylmercaptopurine

MRI Magnetic Resonance Imaging

NCGS Non-Coeliac Gluten Sensitivity

PET Positron emission tomography

POCT Point-of-care test

PPV Positive predictive value

Pre-EATL Low-grade lymphoma

QoL Quality of Life

RCD Refractory Coeliac disease

SNCD Seronegative Coeliac disease

SNP Single nucleotide polymorphism

SR- Slow release

T1DM Type I diabetes mellitus

TCRγ T cell receptor γ

6-TGN 6-thioguanine nucleotides

TG (2,3,6) Tissue Transglutaminase 2,3,6

ULN Upper limit of normal

VA Villous Atrophy

VCE Video capsule endoscopy

WA Wheat allergy

Supplement 3: Acknowledgement

The guideline is been endorsed by the Association of European Coeliac Societies (AOECS) as a representative of coeliac patients organizations.

Supplement 4: Expert committee

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Professor Lundin: KEAL has been involved in clinical trials conducted by Alvine Pharmaceutical, Cellimune and Dr. Falk Pharma.

The other authors declare that there is no conflict of interest.

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Supplement 7: References

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