9. aks Sommerschule, 01.08.2015
Bregenz, Kloster Mehrerau

Guidelines über Guidelines

Prof. Heinz Drexel, MD, FESC, FAHA
Abteilung für Innere Medizin und Kardiologie &
VIVIT Institut am Akademischen Lehrkrankenhaus Feldkirch, A
Private Universität im Fürstentum Liechtenstein, Triesen, FL
Drexel University College of Medicine, Philadelphia, PA, USA
Past-Präsident der Österreichischen Diabetesgesellschaft 2012-2013

Disclosure

Kein Interessenskonflikt;
Akademisches Referat.

Outline

1. **Definition**
2. Persönlicher Zugang
3. Entwicklungsschritte von Guidelines
4. Ebenen von Guidelines
5. Beispiele a) Lipidtherapie
   b) Infektiöse Endokarditis
   c) Diabetes mellitus Typ II
6. Vor- und Nachteile von Guidelines

Definition - Was ist eine Leitlinie (Guideline)?

„Leitlinien sind systematisch entwickelte Aussagen, welche die Entscheidungsfindung von Arzt und Patient unterstützen, um eine angemessene Gesundheitsversorgung bei spezifischen klinischen Gegebenheiten zu gewährleisten.“

(Institute of Medicine comittee to Advice the Public Health Service on Practice Guidelines, USA)

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Mein persönlicher Zugang als Task Force Mitglied

ESC/EAS Guidelines for the management of dyslipidaemias / 2011 → 2015

The Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and the European Atherosclerosis Society (EAS)

Authors/Task Force Members: Željko Reiner* (ESC Chairperson) (Croatia) Alberico L. Catapano* (EAS Chairperson)* (Italy), Guy De Backer (Belgium), Ian Graham (Ireland), Marja-Riitta Taskinen (Finland), Olov Wiklund (Sweden), [redacted], M. John Chapman (France), [redacted], Gabriele Riccardi (Italy), [redacted], David Wood (UK).

Heinz Drexel (Austria), Arno Hoes (The Netherlands), Catriona Jennings (UK), Ulf Landmesser (Germany), Terje Rolf Pedersen (Norway), Lale Tokgözoglu (Turkey), Monique Verschuren (The Netherlands), Charalambos Vlachopoulos (Greece), Jose Zamorano (Spain), Therese Cooney (Ireland)

Mein persönlicher Zugang als Reviewer: Guidelines Infective Endocarditis

Von:	Nathalie CAMERON <ncameron@escardio.org>
Gesendet:	Mittwoch, 22. Juli 2015 18:00
Cc:	Veronica DEAN; Catherine DESPRES; Myriam LAFAY; Laetitia FLOURET
Betreff:	2015 ESC Guidelines for the management of infective endocarditis - Review process feedback

The **2015 ESC Guidelines for the management of infective endocarditis** have entered their publication phase. This phase is the final step before publication and presentation which is scheduled to take place during the ESC Congress 2015 in London. All documents related to these guidelines are still confidential until publication of the full text, as specified in the confidentiality form you all signed. The publication date is planned to be the opening day of the ESC Congress on Saturday 29 August 2015, morning. You will then be able to download the final version of the guidelines full text from the ESC Web Site.

All documents on this platform are still confidential until publication of the full text, as specified in the confidentiality form you all signed.

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Entwicklungsschritte von Guidelines: Beispiel Task Force Dyslipidaemias

1. Verteilung der Aufgaben (Oktober 2014)
2. Änderung gegenüber 2011 (Dezember 2014)
3. Vorläufiger Draft (Februar 2015)
4. Weiteres Meeting, falls nötig
5. Reviewphase
6. Revision mit Berücksichtigung der Reviews
7. Revidierte Version an Reviewer
8. Publikationsphase

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„Levels of Evidence“

Level of Evidence A	Data derived from multiple randomized clinical trials or meta-analyses.
Level of Evidence B	Data derived from a single randomized clinical trial or large non-randomized studies.
Level of Evidence C	Consensus of opinion of the experts and/ or small studies, retrospective studies, registries.

Eur Heart J 2011; 32: 2999-3054.

„Classes of Recommendation“

Classes of recommendations	Definition	Suggested wording to use
Class I	Evidence and/or general agreement that a given treatment or procedu… is beneficial, useful, effecti…	
Class II	Conflicting ev… diver…	
Cla…	*…ncacy.*	Should be considered
Class …	*…ss/efficacy is less well …tablished by evidence/opinion.*	May be considered
Class III	Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful.	Is not recommended

Logische Kombination:
Level A, Class I
Level C, Class III

Eur Heart J 2011; 32: 2999-3054.

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LDL-Cholesterin: ESC Guidelines

ESC/EAS Guidelines 2011

Therapie-Empfehlungen für LDL-C Zielwerterreichung

Recommendations	Class[a]	Level[b]	Ref[c]
In patients at VERY HIGH CV risk (established CVD, type 2 diabetes, type 1 diabetes with target organ damage, moderate to severe CKD or a SCORE level ≥10%) the LDL-C goal is <1.8 mmol/L (less than ~70 mg/dL) and/or ≥50% LDL-C reduction when target level cannot be reached.	I	A	15, 32, 33
In patients at HIGH CV risk (markedly elevated single risk factors, a SCORE level ≥5 to <10%) an LDL-C goal <2.5 mmol/L (less than ~100 mg/dL) should be considered.	IIa	A	15, 16, 17
In subjects at MODERATE risk (SCORE level >1 to ≤5%) an LDL-C goal <3.0 mmol/L (less than ~115 mg/dL) should be considered.	IIa	C	-

Reiner Z et al. European Heart Journal 2011; 32:1769–1818.

ESC/EAS Guidelines 2011

VERY HIGH RISK

LDL-C <70 mg/dl bzw.
>50% Reduktion

bei KHK, PAVK, Insult
Typ 2 Diabetes
Niereninsuffizienz

Reiner Z et al. European Heart Journal 2011; 32:1769–1818.

ESC/EAS Guidelines 2011

HIGH RISK

LDL-C <100 mg/dl

bei

5-10% SCORE 10a Risiko für CV Tod

Reiner Z et al. European Heart Journal 2011; 32:1769–1818.

ESC/EAS Guidelines 2011

MODERATE RISK

LDL-C <112 mg/dl

bei
1-5% SCORE 10a Risiko
für CV Tod

Reiner Z et al. European Heart Journal 2011; 32:1769–1818.

ESC/EAS Guidelines 2011

LOW RISK

LDL-C

< 100 mg/dl	**→ OK**
100-190 mg/dl	**→ Lebensstil-Maßnahmen**
> 190 mg/dl	**→ Medikamente erwägen**

SCORE < 1%
für CV Tod (10a Risiko)

Reiner Z et al. European Heart Journal 2011; 32:1769–1818.

LDL-Cholesterin:
ACC/AHA Guidelines

Amerikanische Guidelines

ELSEVIER

Journal of the American College of Cardiology

Available online 12 November 2013

In Press, Accepted Manuscript — Note to users

2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults : A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines

ACC/AHA Guidelines – Wichtigste Änderungen

Weithin angewandte ATPIII Guideline wird ersetzt (National Heart, Lung and Blood Institutes, 2004).

Wichtigste Änderung:

- **Ärzte beginnen mit moderat- oder hochintensiver Statintherpie ohne Titration auf einen spezifischen LDL-C Zielwert.**
- **Lipidmessungen werden zur Abschätzung der Compliance benötigt, nicht zur Überprüfung einer speziellen LDL-C Zielwerterreichung.**

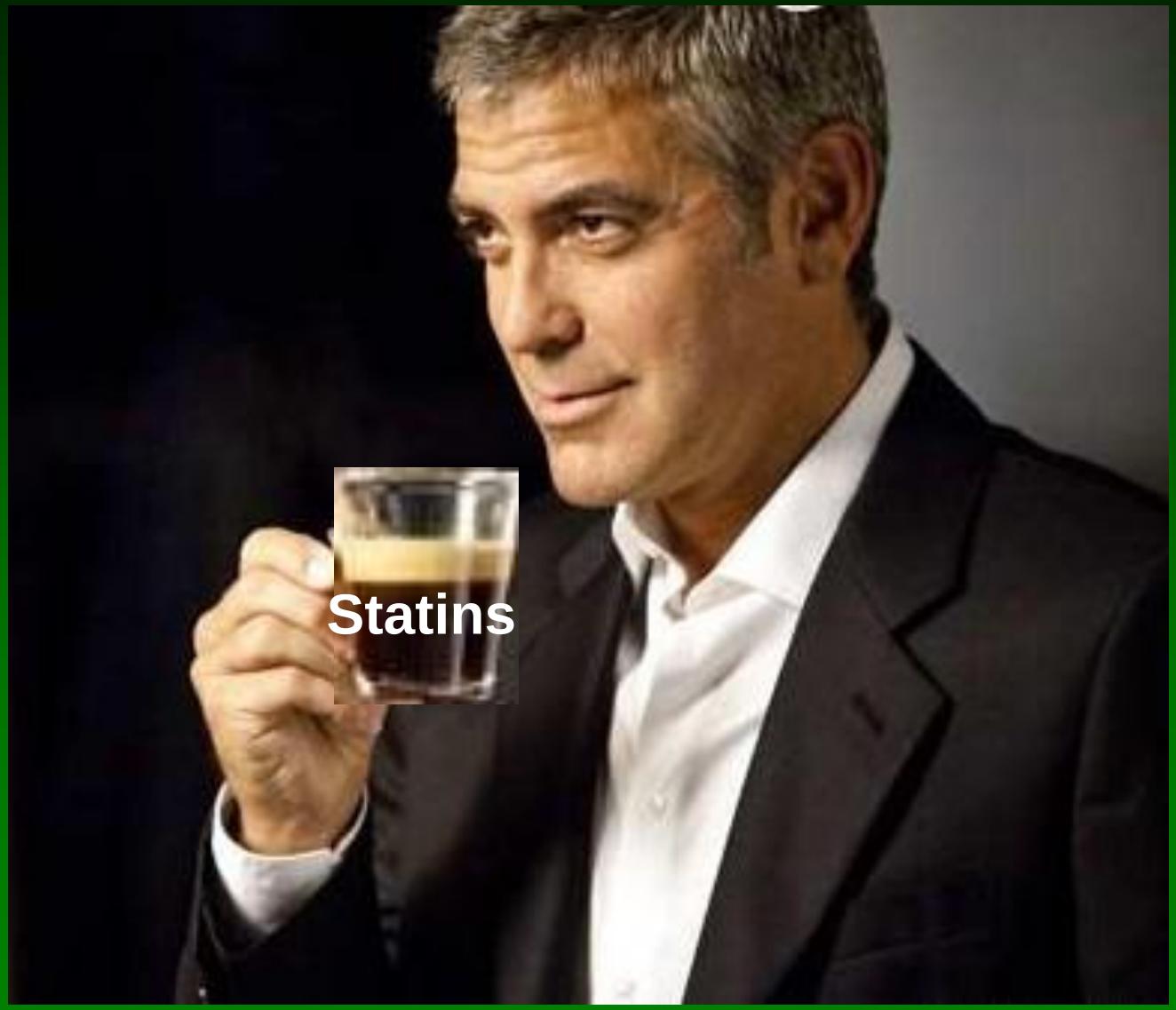
Stone NJ et al. J Am Coll Cardiol 2014; 63: 2889-2934.

Lipidsenker:
2 Philosophien der Guidelines

Europäische Philosophie: Zielwerte

Amerikanische Philosophie: Intervention, "Fire und Forget Strategie"

Statins, what else?



Paradigmenwechsel?

November 2014: IMPROVE-IT

IMPROVE-IT

Die wichtigste Lipidstudie des letzten Jahres

- 18.144 Patienten mit ACS
- Randomisiert zu
  - Simvastatin 40-80 mg/d vs.
  - Simvastatin 40-80 mg/d + Ezetimibe 10 mg
- Follow-up: 6 Jahre

presented at ACC 2015

Studiendesign

IMPROVE-IT

Patients stabilized post ACS ≤ 10 days:
LDL-C 50–125*mg/dL (or 50–100**mg/dL if prior lipid-lowering Rx)

*3.2mM
**2.6mM

N=18,144

Standard Medical & Interventional Therapy

Simvastatin 40 mg

Uptitrated to Simva 80 mg if LDL-C > 79 (adapted per FDA label 2011)

Ezetimibe / Simvastatin 10 / 40 mg

Follow-up Visit Day 30, every 4 months

90% power to detect ~9% difference

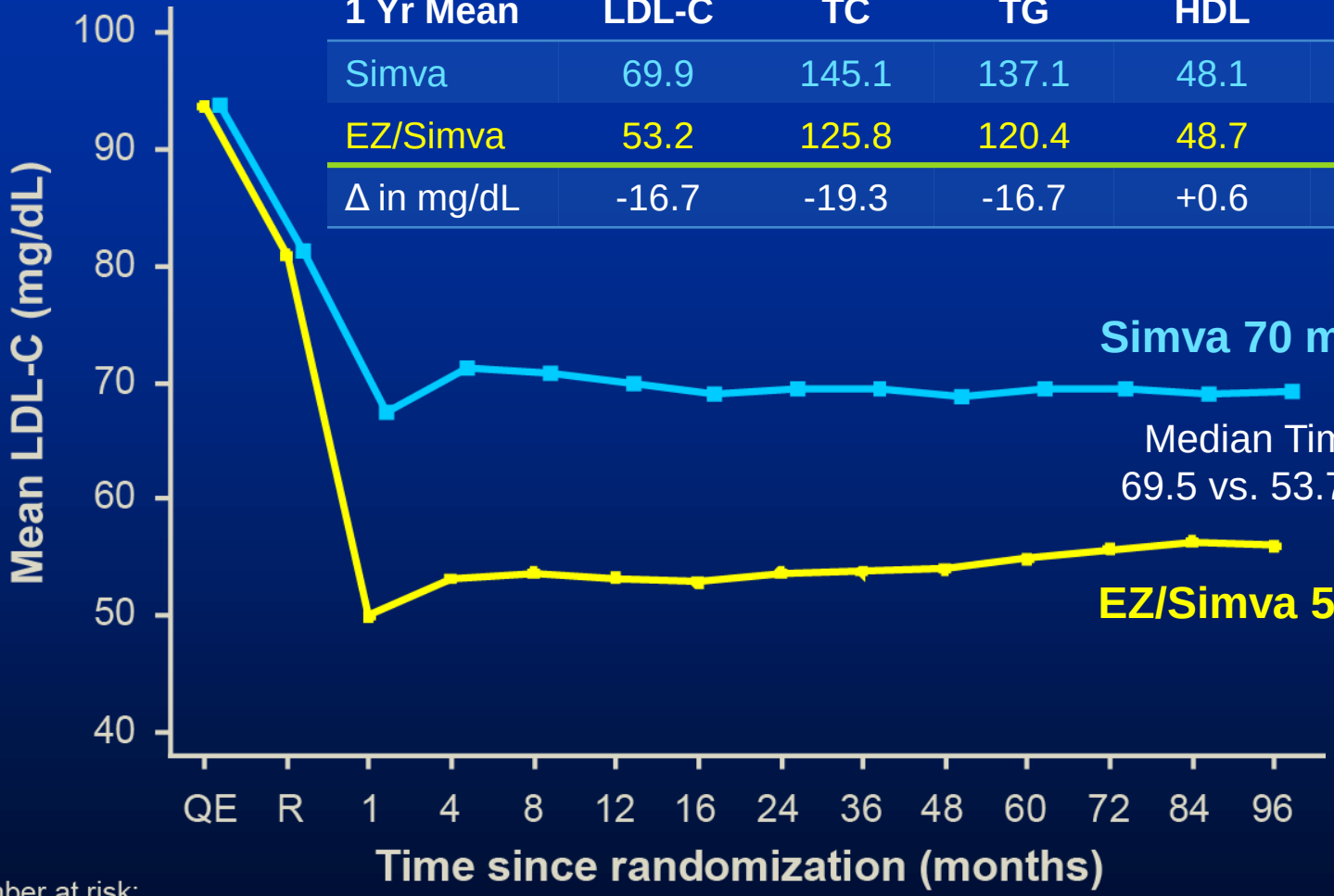
Duration: Minimum 2 ½-year follow-up **(at least 5250 events)**

Primary Endpoint: CV death, MI, hospital admission for UA, coronary revascularization (≥ 30 days after randomization), or stroke

Cannon CP AHJ 2008;156:826-32; Califf RM NEJM 2009;361:712-7; Blazing MA AHJ 2014;168:205-12

LDL-C and Lipidänderung

1 Yr Mean	LDL-C	TC	TG	HDL	hsCRP
Simva	69.9	145.1	137.1	48.1	3.8
EZ/Simva	53.2	125.8	120.4	48.7	3.3
Δ in mg/dL	-16.7	-19.3	-16.7	+0.6	-0.5

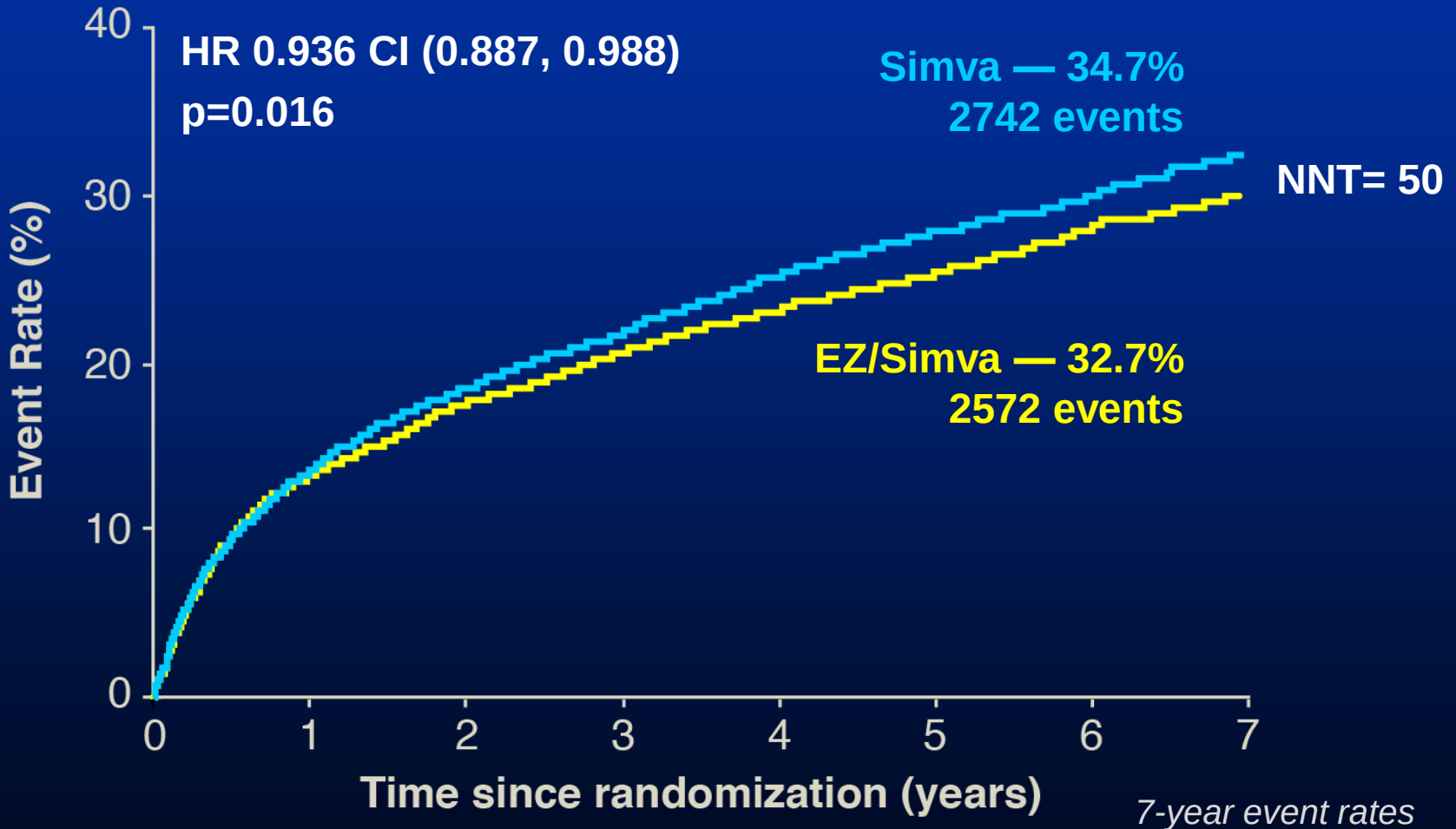


Number at risk:

EZ/Simva	8990	8889	8230	7701	7264	6864	6583	6256	5734	5354	4508	3484	2608	1078
Simva	9009	8921	8306	7843	7289	6939	6607	6192	5684	5267	4395	3387	2569	1068

Primärer Endpunkt — ITT

Cardiovascular death, MI, documented unstable angina requiring rehospitalization, coronary revascularization (≥30 days), or stroke



7-year event rates

IMPROVE-IT: Fazit

- **Die LDL-C Senkung entscheidet!**
- **LDL-C: noch niedriger ist noch besser**
- **Ezetimibe ist wirksam und sicher**

presented at ACC 2015

Europäische Guidelines 2016

- Zielwerte bleiben
- Keine Fire and Forget - Strategie
- Keine Dosiserniedrigung bei niedrigem LDL-C
- … vertraulich

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ESC Guidelines Infektiöse Endokarditis

European Heart Journal (2009) **30**, 2369–2413
doi:10.1093/eurheartj/ehp285

ESC GUIDELINES

Guidelines on the prevention, diagnosis, and treatment of infective endocarditis (new version 2009)

The Task Force on the Prevention, Diagnosis, and Treatment of Infective Endocarditis of the European Society of Cardiology (ESC)

Endorsed by the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) and by the International Society of Chemotherapy (ISC) for Infection and Cancer

Authors/Task Force Members: Gilbert Habib (Chairperson) (France)*, Bruno Hoen (France), Pilar Tornos (Spain), Franck Thuny (France), Bernard Prendergast (UK), Isidre Vilacosta (Spain), Philippe Moreillon (Switzerland), Manuel de Jesus Antunes (Portugal), Ulf Thilen (Sweden), John Lekakis (Greece), Maria Lengyel (Hungary), Ludwig Müller (Austria), Christoph K. Naber (Germany), Petros Nihoyannopoulos (UK), Anton Moritz (Germany), Jose Luis Zamorano (Spain)

ESC Committee for Practice Guidelines (CPG): Alec Vahanian (Chairperson) (France), Angelo Auricchio (Switzerland), Jeroen Bax (The Netherlands), Claudio Ceconi (Italy), Veronica Dean (France), Gerasimos Filippatos (Greece), Christian Funck-Brentano (France), Richard Hobbs (UK), Peter Kearney (Ireland), Theresa McDonagh (UK), Keith McGregor (France), Bogdan A. Popescu (Romania), Zeljko Reiner (Croatia), Udo Sechtem (Germany), Per Anton Sirnes (Norway), Michal Tendera (Poland), Panos Vardas (Greece), Petr Widimsky (Czech Republic)

Habib G et al. European Heart Journal 2009; 30: 2369–2413.

ESC Guidelines Infektiöse Endokarditis

Table 17 Proposed antibiotic regimens for initial empirical treatment of infective endocarditis. (before or without pathogen identification)

Antibiotic	Dosage and route	Duration (weeks)	Level of evidence	Comments
Native valves				
Ampicillin-Sulbactam, *or*	12 g/day i.v. in 4 doses	4–6	IIb C	Patients with blood-culture negative IE should be treated in consultation with an infectious disease specialist.
Amoxicillin-Clavulanate, *with*	12 g/day i.v. in 4 doses	4–6	IIb C	
Gentamicin[a]	3 mg/kg/day i.v. or i.m. in 2 or 3 doses.	4–6		
Vancomycin[b] *with*	30 mg/kg/day i.v. in 2 doses	4–6	IIb C	For patients unable to tolerate β-lactams.
Gentamicin[a] *with*	3 mg/kg/day i.v. or i.m. in 2 or 3 doses.	4–6		
Ciprofloxacin	1000 mg/day orally in 2 doses or 800 mg/day i.v. in 2 doses	4–6		Ciprofloxacin is not uniformly active on *Bartonella* spp. Addition of doxycycline (see *Table 16*) is an option if *Bartonella* spp. is likely.

Habib G et al. European Heart Journal 2009; 30: 2369–2413.

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ESC Guidelines Diabetes Mellitus

European Heart Journal (2013) **34**, 3035–3087
doi:10.1093/eurheartj/eht108

ESC GUIDELINES

ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD

The Task Force on diabetes, pre-diabetes, and cardiovascular diseases of the European Society of Cardiology (ESC) and developed in collaboration with the European Association for the Study of Diabetes (EASD).

Authors/Task Force Members: Lars Rydén* (ESC Chairperson) (Sweden), Peter J. Grant* (EASD Chairperson) (UK), Stefan D. Anker (Germany), Christian Berne (Sweden), Francesco Cosentino (Italy), Nicolas Danchin (France), Christi Deaton (UK), Javier Escaned (Spain), Hans-Peter Hammes (Germany), Heikki Huikuri (Finland), Michel Marre (France), Nikolaus Marx (Germany), Linda Mellbin (Sweden), Jan Ostergren (Sweden), Carlo Patrono (Italy), Petar Seferovic (Serbia), Miguel Sousa Uva (Portugal), Marja-Riita Taskinen (Finland), Michal Tendera (Poland), Jaakko Tuomilehto (Finland), Paul Valensi (France), Jose Luis Zamorano (Spain)

ESC Committee for Practice Guidelines (CPG): Jose Luis Zamorano (Chairperson) (Spain), Stephan Achenbach (Germany), Helmut Baumgartner (Germany), Jeroen J. Bax (Netherlands), Héctor Bueno (Spain), Veronica Dean (France), Christi Deaton (UK), Çetin Erol (Turkey), Robert Fagard (Belgium), Roberto Ferrari (Italy), David Hasdai (Israel), Arno W. Hoes (Netherlands), Paulus Kirchhof (Germany UK), Juhani Knuuti (Finland), Philippe Kolh (Belgium), Patrizio Lancellotti (Belgium), Ales Linhart (Czech Republic), Petros Nihoyannopoulos (UK), Massimo F. Piepoli (Italy), Piotr Ponikowski (Poland), Per Anton Sirnes (Norway), Juan Luis Tamargo (Spain), Michal Tendera (Poland), Adam Torbicki (Poland), William Wijns (Belgium), Stephan Windecker (Switzerland).

Rydén L et al. European Heart Journal 2013; 34: 3035–3087.

ESC Guidelines Diabetes Mellitus

Glycaemic control in diabetes			
Recommendations	**Class [a]**	**Level [b]**	**Ref. [c]**
It is recommended that glucose lowering is instituted in an individualized manner taking duration of DM, co-morbidities and age into account.	I	C	-
It is recommended to apply tight glucose control, targeting a near-normal HbA_{1c} (<7.0% or <53 mmol/mol) to decrease microvascular complications in T1DM and T2DM.	I	A	151–153, 155, 159
A HbA_{1c} target of ≤7.0% (≤53 mmol/mol) should be considered for the prevention of CVD in T1 and T2 DM.	IIa	C	-
Basal bolus insulin regimen, combined with frequent glucose monitoring, is recommended for optimizing glucose control in T1DM.	I	A	151, 154
Metformin should be considered as first-line therapy in subjects with T2DM following evaluation of renal function.	IIa	B	153

Rydén L et al. European Heart Journal 2013; 34: 3035–3087.

Therapie des Typ 2 Diabetes: Empfehlungen der ADA & EASD

1. Wahl:

- Metformin

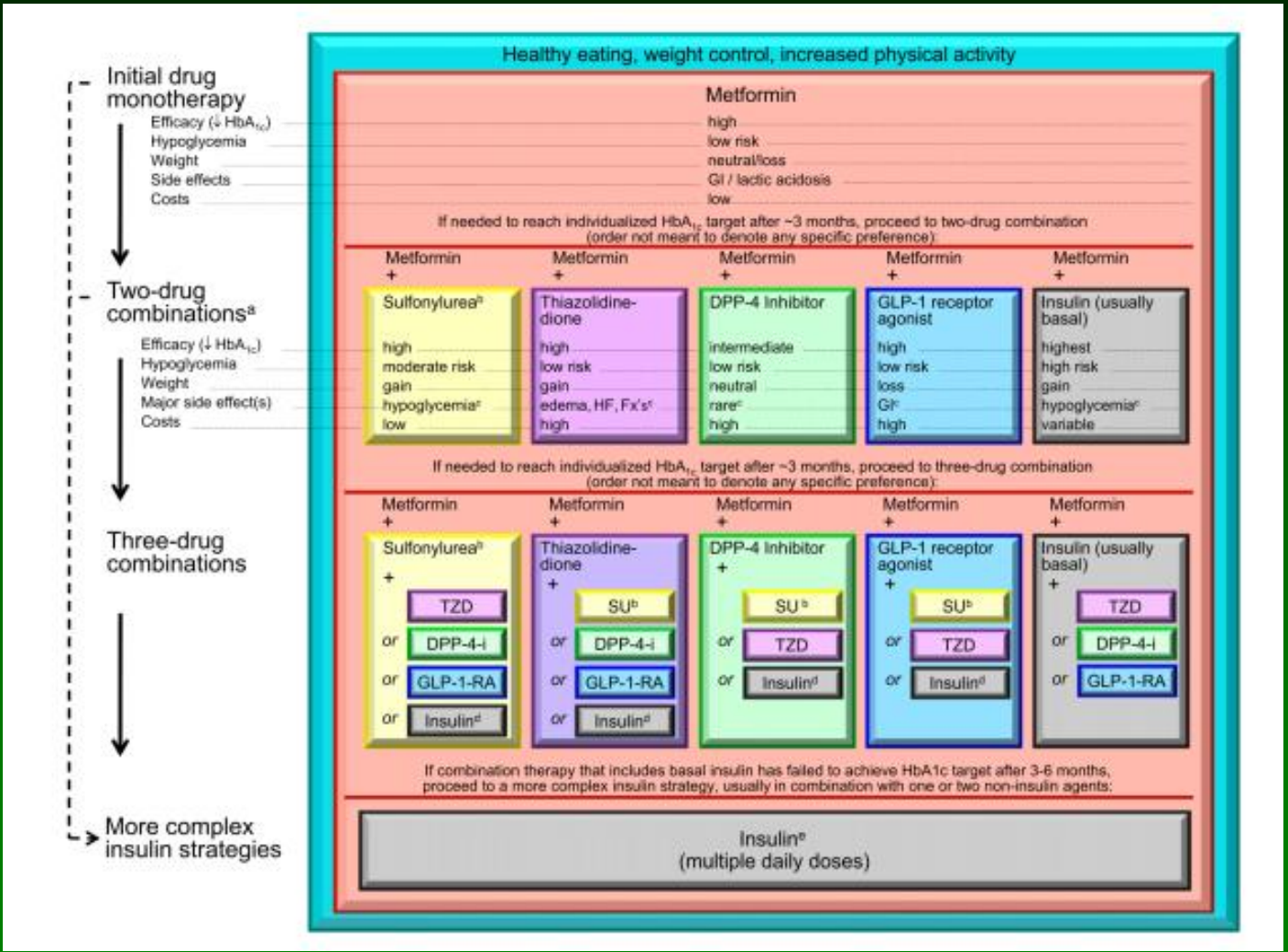
2. Wahl: gleichwertig

- DPP-4-Inhibitoren
- Pioglitazon
- Glinide
- Sulfonylharnstoffe
- SGLT-2-Inhibitoren

3. Wahl:

- Insulin
- GLP1-Agonisten

Metformin: Basis der Diabetestherapie



Inzucchi SE et al. Diabetes Care 2012 ; 35:1364-79.

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Vor- und Nachteile von Guidelines

Vorteile:

1.) Evidenzbasierte Therapie

2.) Klare Empfehlung

3.) Impact factor des Journals steigt

Nachteile:

1.) Oft zu umfangreich für die Praxis

2.) Häufige Änderungen

3.) Zuviel Regionalisierung

Zusammenfassung

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SAVE THE DATE

EUROPEAN SOCIETY OF CARDIOLOGY®

Cardiovascular Pharmacotherapy
ESC Working Group

UFL Private Universität im Fürstentum Liechtenstein

VIVIT
Vorarlberg Institute for Vascular Investigation & Treatment

VORPROGRAMM

„Update Cardiovascular Pharmacotherapy“

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15. – 16. Oktober 2015

Gemeindessaal Triesen, Triesen, Liechtenstein

9. aks Sommerschule, 01.08.2015
Bregenz, Kloster Mehrerau

Guidelines über Guidelines

Prim. o.Univ.Prof Dr. Dr. h.c. **Heinz Drexel**
Abteilung für Innere Medizin und Kardiologie &
VIVIT Institut am Akademischen Lehrkrankenhaus Feldkirch, A
Private Universität im Fürstentum Liechtenstein, Triesen, FL
Drexel University College of Medicine, Philadelphia, PA, USA
Past-President der Österreichischen Diabetesgesellschaft