HOW DOES TRIUMEQ® (DTG + ABC/3TC) COMPARE TO ATRIPLA® (EFV/FTC/TDF) IN TREATMENT-NAÏVE PATIENTS?

SINGLE STUDY DATA UP TO 144 WEEKS

(Based on data from 144 week presentation)

In studies supporting TRIUMEQ®, DTG 50 mg + ABC 600 mg/3TC 300 mg were used. Bioequivalence has been demonstrated.
ATRIPLA® may not be licensed for initial use in all markets.

Triumeq®
dolutegravir/abacavir/lamivudine

THERAPEUTIC INDICATIONS

- TRIUMEQ®† is indicated for the treatment of Human Immunodeficiency Virus (HIV) infected adults and adolescents above 12 years of age weighing at least 40 kg
- Hypersensitivity reaction is an uncommon but potentially life-threatening adverse event of abacavir, causally linked to carriage of the HLA-B*5701 genetic allele
- Before initiating treatment with TRIUMEQ®, screening for carriage of the HLA-B*5701 allele should be performed in any HIV-infected patient, irrespective of racial origin
- TRIUMEQ® should never be initiated in patients with a positive HLA-B*5701 status, nor in patients with a negative HLA-B*5701 status who had a suspected abacavir hypersensitivity reaction on a previous abacavir-containing regimen

† In studies supporting TRIUMEQ®, DTG 50 mg + ABC 600 mg/3TC 300 mg were used. Bioequivalence has been demonstrated.

PHASE III DOLUTEGRAVIR TRIALS IN TREATMENT-NAÏVE ADULT SUBJECTS WITH HIV

N=833	Non-inferiority, randomised, double-blind, double-dummy, multicentre study of: TRIUMEQ® (QD) with ATRIPLA® placebo ATRIPLA® (QD) with TRIUMEQ® placebo	SINGLE	TRIUMEQ®* *vs* ATRIPLA®
N=822	Non-inferiority, randomised, double-blind, double-dummy, multicentre study of: TIVICAY™ (QD) plus ISENTRESS® placebo (BID) + 2 NRTIs ISENTRESS® (BID) plus TIVICAY™ placebo (QD) + 2 NRTIs	SPRING-2	TIVICAY™ *vs* ISENTRESS®
N=484	Non-inferiority, randomised, active-controlled, multicentre, open-label study of: TIVICAY™ (QD) + 2 NRTIs PREZISTA® (DRV/r [800†/100 mg] QD) + 2 NRTIs	FLAMINGO	TIVICAY™ *vs* PREZISTA®
N=65	Randomized, single-centre, 2-part, open-label study of the single-dose PK of: TRIUMEQ® (QD) ± Food ABC/3TC (600/300 mg) + DTG (50mg)		(PK) TRIUMEQ® *vs* DTG + ABC/3TC components

†Given as 2 x 400 mg tablets

*In studies supporting TRIUMEQ®, DTG 50 mg + ABC 600 mg/3TC 300 mg were used. Bioequivalence has been demonstrated.

ATRIPLA® is a registered trademark of Bristol-Myers Squibb & Gilead Sciences, LLC

TIVICAY™ is a registered trademark of the ViiV Healthcare Group of Companies

ISENTRESS® is a registered trademark of Merck & Co., Inc.

PREZISTA® is a registered trademark of Tibotec Pharmaceuticals Ltd.

Walmsley S, et al. *N Engl J Med* 2013; 369:1807-18

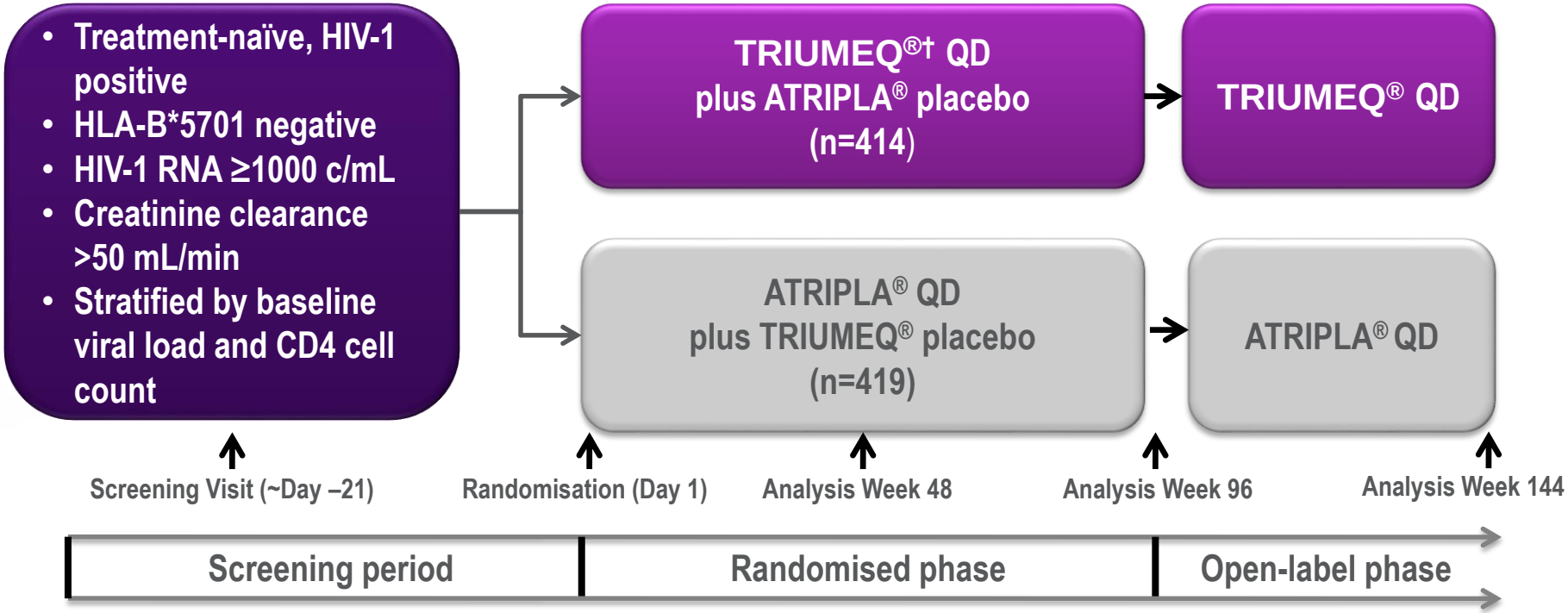
Raffi F, et al. *Lancet* 2013; 381:735–43

Raffi F, et al. *Lancet Infect Dis* 2013; 13:927-35

Clotet B, et al. *Lancet* 2014; 383:2222-31

Weller S, et al. *JAIDS* 2014;66:393-398

SINGLE STUDY DESIGN



Primary endpoint: Proportion with HIV-1 RNA <50 c/mL at Week 48, FDA snapshot analysis (-10% non-inferiority margin with pre-specified tests for superiority)

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Adapted from Walmsley S, et al. *N Engl J Med* 2013; 369:1807-18

BASELINE CHARACTERISTICS

Characteristic	TRIUMEQ®* QD (n=414)	ATRIPLA® QD (n=419)
Median age, years (range)	36 (18-68)	35 (18-35)
Female, n (%)	67 (16)	63 (15)
African American / African Heritage, n (%)	98 (24)	99 (24)
CDC class C, n (%)	18 (4)	17 (4)
Baseline HIV-1 RNA		
Median (log_{10} c/mL)	4.67	4.70
>100,000 c/mL, n (%)	134 (32)	131 (31)
Median CD4 cell count, cells/mm^3	334.5	339.0
<200, %	14	14
200 to <350, %	39	38
350 to <500, %	32	31
≥500, %	15	17

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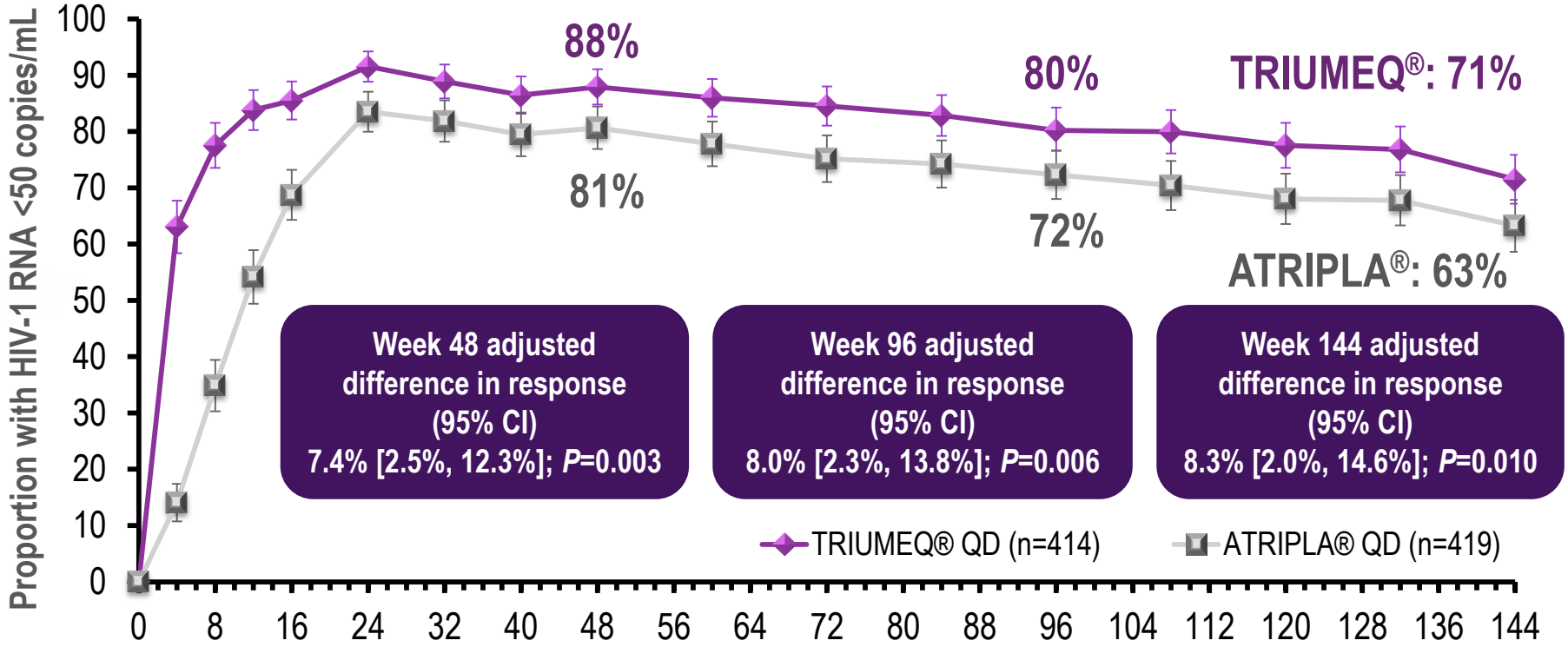
Adapted from Walmsley S, et al. *N Engl J Med* 2013; 369:1807-18

Adapted from Walmsley S, et al. *N Engl J Med* 2013; 369:1807-18 (appendix)

TRIUMEQ®* MAINTAINED STATISTICALLY SUPERIOR EFFICACY VS ATRIPLA® UP TO 144 WEEKS

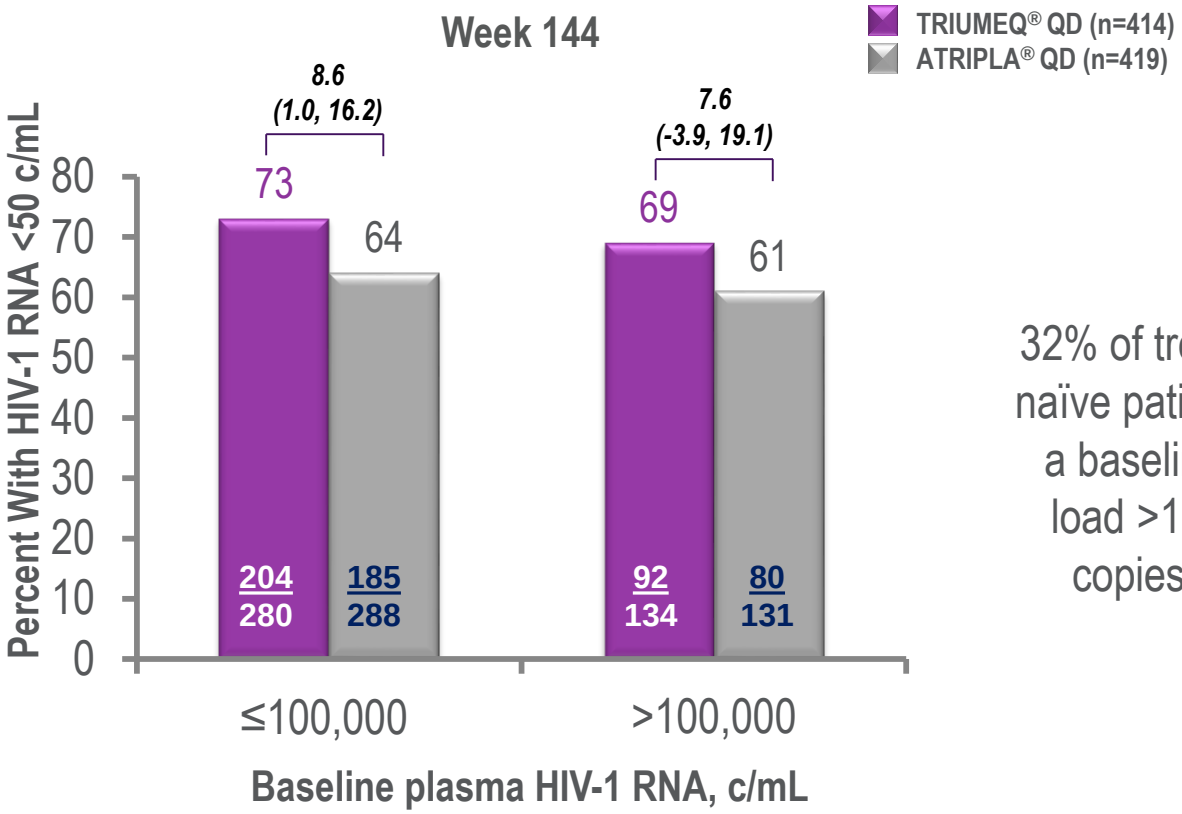
TRIUMEQ® demonstrated statistically superior efficacy vs ATRIPLA® at 48, 96, and 144 weeks
TRIUMEQ® demonstrated rapid suppression of viral load vs ATRIPLA®
(28 days vs 84 days, respectively; *P*<0.0001)



-10% non-inferiority margin with pre-specified tests for superiority
*In studies supporting TRIUMEQ®, DTG 50 mg + ABC 600 mg/3TC 300 mg were used. Bioequivalence has been demonstrated.

TRIUMEQ® Produktresumé 01/17
Adapted from Walmsley S, et al. *N Engl J Med* 2013; 369:1807-18
Adapted from Walmsley S, et al. Poster presented at: 21st CROI 2014. Poster 543
Adapted from Pappa K, et al. Presented at: 54th ICAAC 2014. H-647a

TRIUMEQ®* WAS EFFECTIVE REGARDLESS OF BASELINE VIRAL LOAD



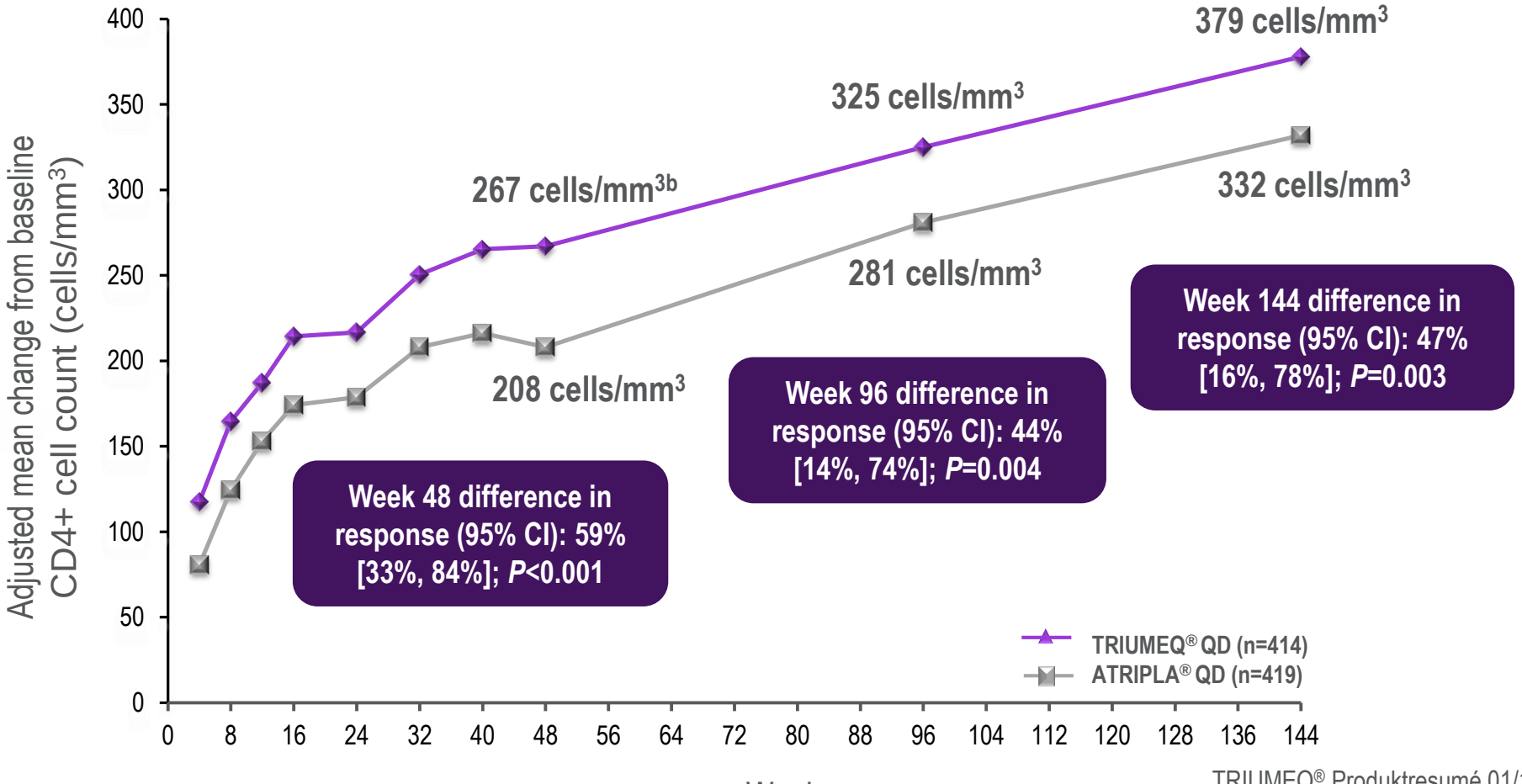
32% of treatment-naïve patients had a baseline viral load >100,000 copies/mL†‡

†P=0.831; ‡test for homogeneity; P value confirms that there is no evidence of heterogeneity in treatment difference across the baseline stratification factors

*In studies supporting TRIUMEQ®, DTG 50 mg + ABC 600 mg/3TC 300 mg were used. Bioequivalence has been demonstrated.

Walmsley S, et al. *N Engl J Med* 2013; 369:1807-18 (appendix)
Adapted from Pappa K, et al. Presented at: 54th ICAAC 2014. H-647a
Adapted from Pappa K, et al. Abstract presented at: 54th ICAAC 2014

TRIUMEQ®* HAD STATISTICALLY SUPERIOR CD4+ T-CELL INCREASES VS ATRIPLA® UP TO 144 WEEKS



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TRIUMEQ® Produktresumé 01/17

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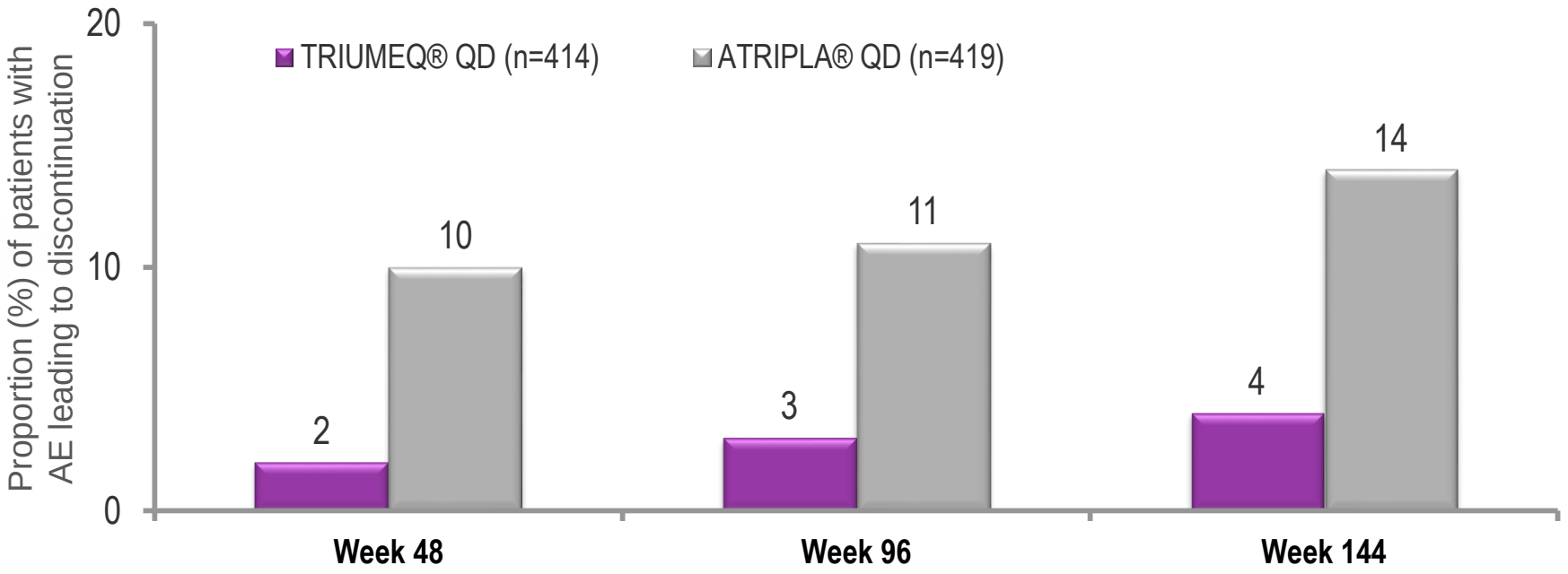
Adapted from Pappa K, et al. Presented at: 54th ICAAC 2014. H-647a

FEWER DISCONTINUATIONS DUE TO ADVERSE EVENTS UP TO 144 WEEKS WITH TRIUMEQ®* VS ATRIPLA®

Discontinuations due to AEs were 4% for TRIUMEQ® vs 14% for ATRIPLA® at Week 144



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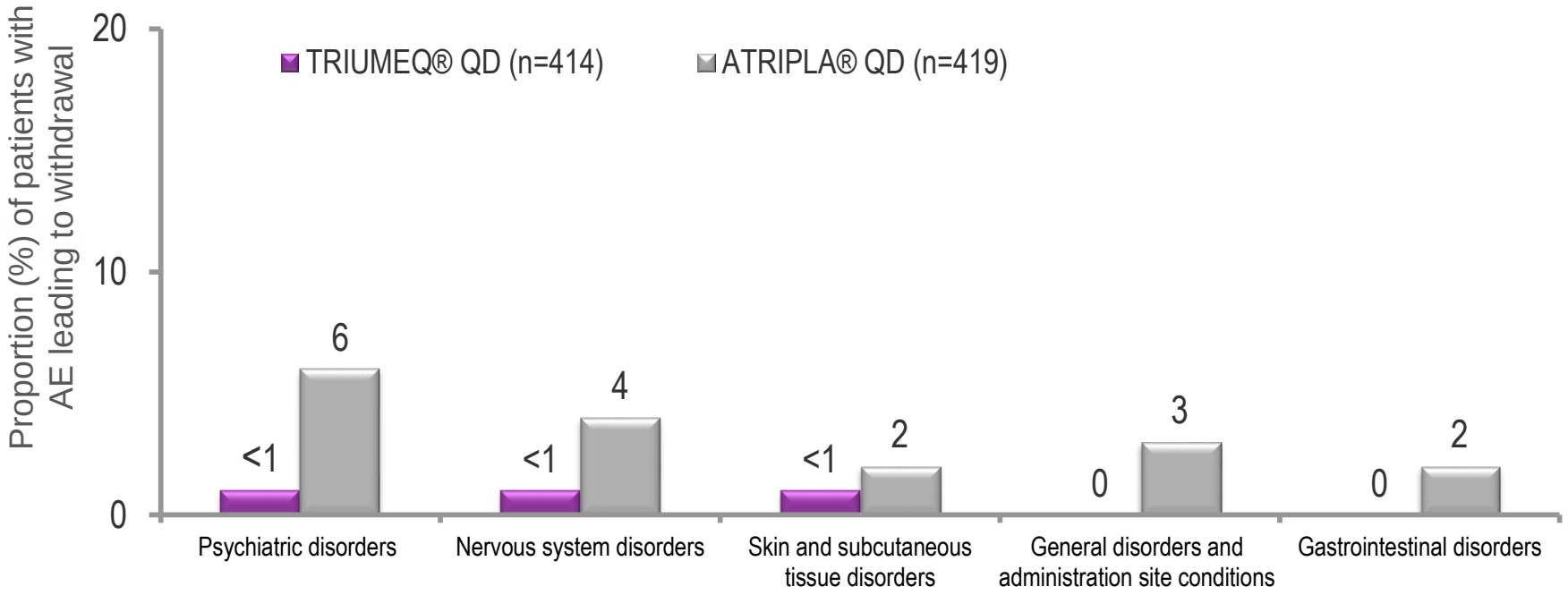
TRIUMEQ®* WAS GENERALLY BETTER TOLERATED VS ATRIPLA® UP TO 144 WEEKS WITH FEWER DISCONTINUATIONS

The incidence of psychiatric or nervous system disorders leading to withdrawal up to 144 weeks was <1% each for TRIUMEQ® and 6%, 4% respectively for ATRIPLA®

Common AEs leading to withdrawal by system organ class (≥2% in either arm)



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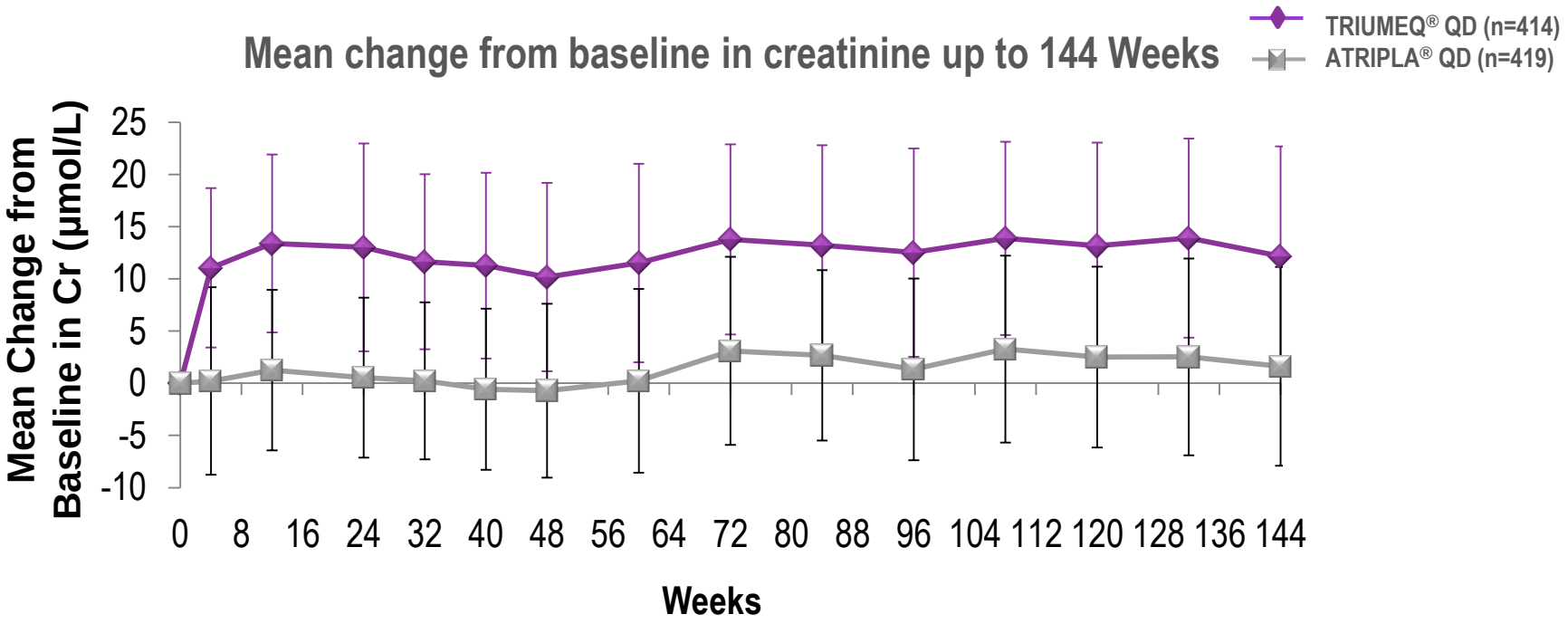
Adapted from Pappa K, et al. Presented at: 54th ICAAC 2014. H-647a

THE EFFECT OF TRIUMEQ®* ON SERUM CREATININE IS NOT CLINICALLY RELEVANT UP TO 144 WEEKS

Small increases in serum creatinine occurred in the first week and remained stable up to 144 weeks
These changes are not considered to be clinically relevant as the glomerular filtration rate is unchanged



*In studies supporting TRIUMEQ®, DTG 50 mg + ABC 600 mg/3TC 300 mg were used. Bioequivalence has been demonstrated.

Koteff J et al. *Br J Clin Pharmacol*. 2013;75(4):990-996
Adapted from Pappa K, et al. Presented at: 54th ICAAC 2014. H-647a

TRIUMEQ®* HAS DEMONSTRATED A HIGH BARRIER TO RESISTANCE TO DATE

No INI or NRTI resistance seen with TRIUMEQ® up to 144 weeks

	TRIUMEQ® QD (n=414)			ATRIPLA® QD (n=419)		
	Week 48	**Week 96**	**Week 144**	**Week 48**	**Week 96**	**Week 144**
INI-resistant major substitution	0	0**	0**	N/A	N/A	N/A
NRTI major mutations	0	0	0	1†	1†	1†
NNRTI major mutations	N/A	N/A	N/A	4‡	6††	6††

**E157Q/P polymorphism detected in 1 patient with no significant change in INI phenotypic susceptibility
†Treatment emergent NRTI mutations detected: K65R
‡Treatment-emergent NNRTI mutations detected: K101E (n=1), K103K/N (n=1), G190G/A (n=1) and K103N+G190G/A (n=1)
†† Treatment-emergent NNRTI mutations detected: K101E (n=1); K103N (n=1); K103K/N (n=2) , G190A (n=1) ; K103N+G190A (n=1)
*In studies supporting TRIUMEQ®, DTG 50 mg + ABC 600 mg/ 3TC 300 mg were used. Bioequivalence has been demonstrated.

TRIUMEQ® Produktresumé 01/17
Adapted from Walmsley S, et al. *N Engl J Med* 2013; 369:1807-18
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Adapted from Walmsley S, et al. Poster presented at: 21st CROI 2014. Poster 543
Adapted from Pappa K, et al. Presented at: 54th ICAAC 2014. H-647a

SINGLE: SUMMARY

- TRIUMEQ®* had statistically superior efficacy vs ATRIPLA®
  - 88% vs 81% remained undetectable at 48 weeks (*P*=0.003)
  - 80% vs 72% remained undetectable at 96 weeks (*P*=0.006)
  - 71% vs 63% remained undetectable at 144 weeks (*P*=0.010)
- TRIUMEQ® is effective regardless of baseline viral load
  - 83% of treatment-naïve patients with HIV-1 RNA >100,000 copies/mL remained undetectable at 48 weeks
  - TRIUMEQ® was still as effective as ATRIPLA® in patients with high baseline viral loads at 96 weeks
  - 69% of treatment-naïve patients with HIV-1 RNA >100,000 copies/mL remained undetectable at 144 weeks
- TRIUMEQ® was generally better tolerated vs ATRIPLA® with fewer discontinuations
  - 2% vs 10% discontinued due to AEs at 48 weeks
  - 3% vs 11% discontinued due to AEs at 96 weeks
  - 4% vs 14% discontinued due to AEs at 144 weeks
- No INI or NRTI resistance up to 144 weeks with TRIUMEQ®
- HLA-B* 5701 testing should be performed before initiating treatment with TRIUMEQ®

*In studies supporting TRIUMEQ®, DTG 50 mg + ABC 600 mg/ 3TC 300 mg were used. Bioequivalence has been demonstrated.

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SUPPLEMENTARY SAFETY INFORMATION

TRIUMEQ®* HAD A LOWER IMPACT ON LIVER CHEMISTRY THAN ATRIPLA® AT WEEK 48

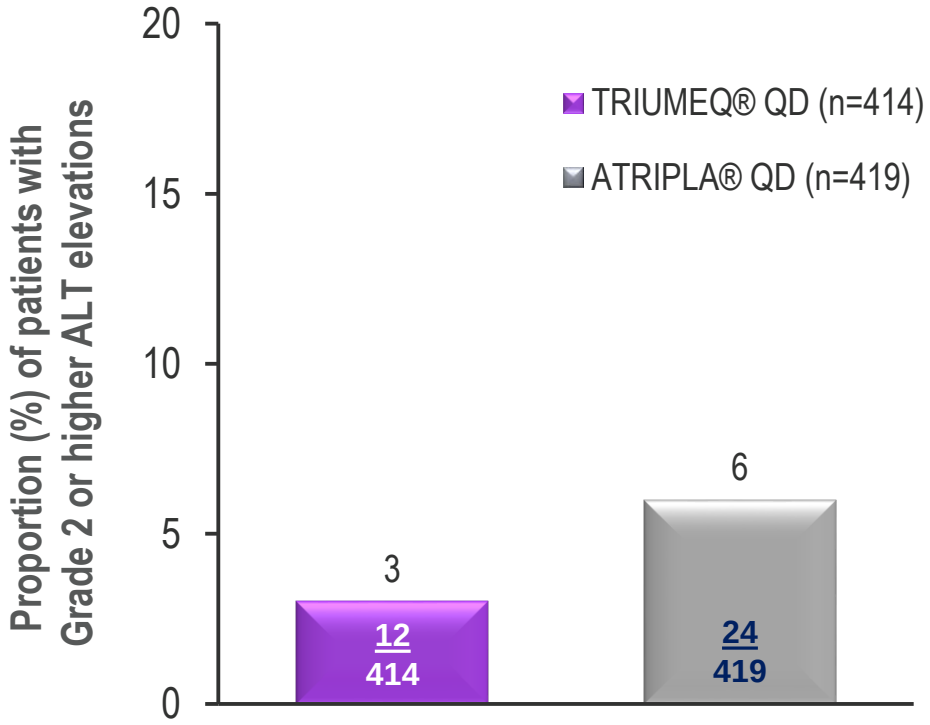
Parameter/Criteria, (%) at Week 48[1]	TRIUMEQ® QD (n=414)	ATRIPLA® QD (n=419)
Subjects meeting ≥1 FDA stopping criteria	10 (2)	39 (9)
ALT ≥20xULN	0	0
ALT ≥5xULN	1 (<1)	2 (<1)
ALT ≥3xULN	5 (1)	15 (4)
Total bilirubin >1.5xULN	3 (<1)	2 (<1)
Alkaline phosphatase >1.5xULN	1 (<1)	19 (5)
ALT and/or AST >3xULN and total bilirubin >1.5xULN	0	0

*In studies supporting TRIUMEQ®, DTG 50 mg + ABC 600 mg/ 3TC 300 mg were used. Bioequivalence has been demonstrated.

Adapted from Walmsley S, et al. 52nd ICAAC. 9-12 Sept 2012. Abstract H-556b

TRIUMEQ®* HAD A LOWER IMPACT ON LIVER CHEMISTRY THAN ATRIPLA® AT WEEK 96

Grade 2 or higher ALT elevations were observed more commonly in the ATRIPLA® arm than in the TRIUMEQ® arm at Week 96



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Adapted from Walmsley S, et al. Poster presented at: 21st CROI 2014. Poster 543

ABBREVIATIONS

- 3TC, lamivudine
- ABC, abacavir
- AE, adverse event
- ALT, alanine amino transferase
- AST, aspartate amino transferase
- BID, twice daily
- c/mL, copies/mL
- CDC, Centres for Disease Control
- Cr, creatinine
- DRV/r, darunavir/ritonavir
- DTG, dolutegravir
- FDA, Food and Drug Administration
- HIV, human immunodeficiency virus
- HSR, hypersensitivity reaction
- INI, integrase inhibitor
- NRTI, nucleoside reverse transcriptase inhibitor
- QD, once daily
- RNA, ribonucleic acid
- ULN, upper limit of normal

MINIMIINFORMATION OCH RAPPORTERING AV BIVERKNINGAR

TRIUMEQ® (dolutegravir/abakavir/lamivudin) Rx, EF, ATC kod J05AR13

▼ Detta läkemedel är föremål för utökad övervakning.

Detta läkemedel är föremål för utökad övervakning.Filmdragerad tablett innehållande 50 mg dolutegravir (som natrium), 600 mg abakavir (som sulfat), 300 mg lamivudin.

Indikation: TRIUMEQ är avsett för behandling av humant immunbristvirus (hiv) hos vuxna och ungdomar över 12 år som väger mer än 40 kg. Innan behandling med abakavirinnehållande läkemedel påbörjas, ska screening för HLA-B*5701-allelen utföras på samtliga hiv-infekterade patienter, oavsett etniskt ursprung. Abakavir ska inte användas till patienter som man vet bär på HLA-B*5701-allelen.

Kontraindikationer: Överkänslighet mot dolutegravir, abakavir eller lamivudin eller mot något hjälpämne. Samtidig administrering av dofetilid.

Varningar och försiktighet: Behandling ska förskrivas av läkare med erfarenhet av behandling av hiv-infektion. Både abakavir och dolutegravir är förenade med en risk för överkänslighetsreaktioner. Överkänslighetsreaktioner har observerats oftare med abakavir, och några har varit livshotande, i sällsynta fall dödliga, när de inte har hanterats på rätt sätt. TRIUMEQ och andra misstänkta preparat måste därför omedelbart sättas ut vid tecken eller symtom på överkänslighetsreaktion. Om behandlingen med TRIUMEQ avslutas på grund av misstänkt överkänslighetsreaktion så får TRIUMEQ eller andra läkemedel som innehåller abakavir eller dolutegravir aldrig sättas in på nytt. *Nedsatt njurfunktion:* TRIUMEQ rekommenderas inte till patienter med kreatininclearance < 50 ml/min. *Nedsatt leverfunktion:* TRIUMEQ rekommenderas inte till patienter med måttligt eller allvarligt nedsatt leverfunktion.

TRIUMEQ rekommenderas inte till patienter med resistens mot integrashämmare eller vid samtidig administrering av efavirenz, nevirapin, rifampicin och tipranavir/ritonavir.

Interaktioner: Faktorer som minskar exponeringen för dolutegravir ska undvikas i närvaro av integrasklassresistens. Detta inkluderar samtidig administrering med läkemedel som minskar exponeringen för dolutegravir (t.ex. magnesium- och aluminiuminnehållande antacida, järn- och kalciumtillskott, multivitaminer och inducerande preparat, etravirin (utan boostade proteashämmare), tipranavir/ritonavir, rifampicin, johannesört och vissa antiepileptika). Dolutegravir ökar koncentrationen av metformin. Dosjustering av metformin ska övervägas vid insättning och utsättning av samtidig administrering av dolutegravir och metformin, för att bevara glykemisk kontroll . Metformin elimineras renalt och det är därför viktigt att kontrollera njurfunktionen vid samtidig administrering av dolutegravir. Denna kombination kan öka risken för laktacidos hos patienter med måttligt nedsatt njurfunktion.

Biverkningar: De vanligaste rapporterade biverkningar som ansågs möjligen eller troligen relaterade till kombinationen dolutegravir och abakavir/lamivudin var illamående (12 %), insomni (7 %), yrsel (6 %) och huvudvärk (6 %). Abakavir-innehållande läkemedel, som TRIUMEQ, ska inte användas till patienter som man vet bär på HLA-B*5701-allelen.

Vid tecken på överkänslighetsreaktion skall TRIUMEQ, omedelbart utsättas.

För fullständig förskrivarinformation, se www.fass.se Datum för översyn av produktresumén 01/2017

TRIUMEQ är ett registrerat varumärke som tillhör företagsgruppen ViiV Healthcare.

Om du vill rapportera en biverkan eller oönskad händelse kontakta biverkningsenheten på GlaxoSmithKline:
Telefon: 08-638 93 00 Postadress: Biverkningsenheten, GlaxoSmithKline, Box 516, 169 29 Solna