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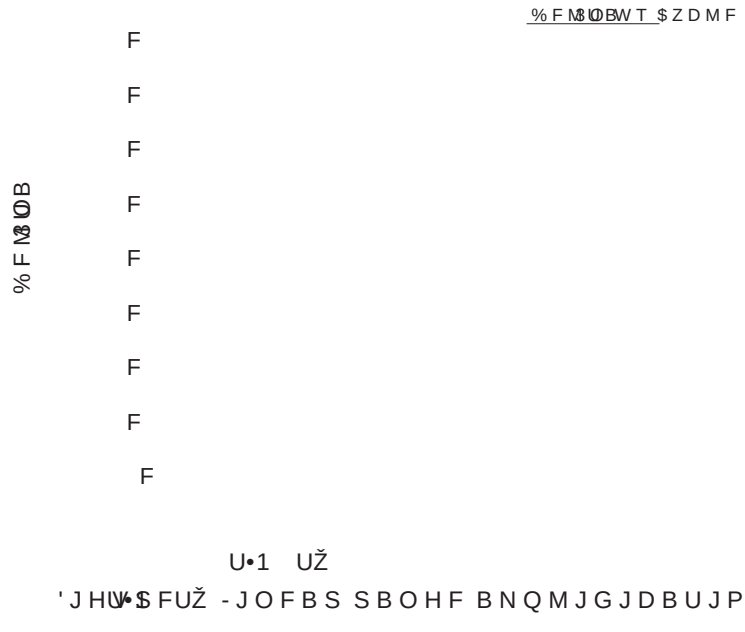
Volume 11 Number 5 September 2019



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分子诊断与治疗杂志

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Clinical application and significance of high sensitivity hepatitis B virus DNA detection

UANE Hie WS Euangxin JS Fengmin*

Department of Kicrobiology $ Gnfectious Disease CenterSchool of Basic Kedical Sciences Peking Sniversity Health Science CenterBei hingChina 100171

ABSTRACT Ouantitative detection of hepatitis B virusHBV DNA can effectively monitor the infection status and antiviral efficacy of HBVthus it has important clinical significance in the diagnosis and evaluation of antiviral efficacy for chronic hepatitis BCHB , Compared with the conventional HBV DNA detection the high Ų senesitivity HBV DNA detection has lower detection limit and a wider linear rangeand has been used as an important indicator for evaluating the virological response and the end point of treatment for CHB patients receiving nucleos t ide analogues in the guidelines of CHB management , Gn this manuscript we review the applications of high Ų sensitivity HBV DNA detection in sceening for occult HBV infection OBG to enhance the safety of blood transfusionsceening for HBV infection before operation to reduce iatrogenic HBV infection sceening for HBV infection before radiotherapy and chemotherapy to reduce the occurrence of HBV reactivationevaluating antiviral efficacy and treatment endpoints to reduce the viral rebound and CHB replase after drug withdrawahd predicting drug resistance mutations in HBeAg negative CHB patients ,

I EW UORDS Hepatitis B virus High Ų sensitivity HBV DNA detectionOccult HBV infection Nucleos t ide analogues

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MBG Ψ FBT BLA ’ ó

MBG ’ [9][11] ɟ 2..7 P_ɡkmlbm Ὸ

Ψ FBT BLA ‟ ˩ ⊿ ’

MBG ۱ ’ [12] ɟ

2..8 MBG τ ε FBT

i FBqAe

Ψ ı ǫ̈ FBT BLA ж Ψ

FBT BLA [13] ɟ ⊿ ɣ ⊿ ה

NCPɐ ẉ PCP ۱ NCPẄ˜

Њ MBG ۱

FBT BLA Y ˩ ⊿ w Ξ Y ẇ

w ɔ ˩ ⊿ Ὸ Ə ε MBG Ã [13] ɟ ғ

۱ Ă ɵ ´ BLA amt_jc l rjw ajmqcb aɡpaЏ

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paBLA Ϛ aaaBLA Ⴖ[m] ɟ ė aaaBЏ

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Ẋ FBT BLA bms`jc

qrp_l bq jɡ l c_p BLA bqjBLA w ę ‟ Ė Ə ε

У ц Ὼ [15][16] ɟ Њ ´

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ʃ ЊA ئ Ė Ϊ Ą

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Ő ɟ ğ Ђ ´ FBT BLA φ ˜

paBLA ۱ - aaaBLA Ὸ ◗ ’ ó ε

MBGɟ ğ ɣ ɔ ЊA MBG O ئ

τ ε FBT i

FBqAe FBT BLA ɳ Њ

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paBLA ۱ - aaaBLA [17][18] ɟ

MBGה ζ Ɑ ė Њ Ї aaaBLA

Ő FBT ζ ӧ ˜ Ш

FBT ɳ Ϊ Ą [19] ɟ Ɠ ӧ

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ϛ MBGה Ɑ ė [2.] ɟ MBG Ά

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Ψ MBG Ὸ ε ...3# ǀ.2# ϛ Њ ה

۸ ....7# ǀ..5# [22] ɟ ă ӧ

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1 , H,

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2 J_g KUgl RWq_mcA_j, GlapcU_qcbqcp jclacmd F@T BL? ugrf ksr_rgmlqgl glbgtgbs_j/6ep cpqmpb fd rUcp amknj agl H,gEm_lqrpmc0 r/02m1j 2ewU2.5,

3 Fmmdl_eQjcc HE@J@cqcXr@_j, RwUnc@fcn _rgrgq_drcprp_lqdsqgml ugrf `jm fcn_rgrgq@H,mlpC_ej r H/eK5c0676 03/157U/161,

4 U_leHUR_leRQFfcscHA_j, BcrdUargmlmd _rgrgq@tgpsqBL?`wnmjwkUcp_qca k_md tmjslrccp `jmmb bmlmpq lce_ qspd_acH,lH GHedcl/a7r7B/41 17U5 177,

5 Af_xmsg jKj_ckpgcqqflMBk Kcr _Mja,aNsjr fcn_rgrgq@tgpsq_q qmspUacmd glc nj_lr pcH,gJ gc/a7r7q1221667./2U0 /24,

6 Tgjj EpCmrrm@js_r P_dmram_N, Ctgbclacd fcn_rgrgq@tgpsqgldcargUmlgln_r rgrgqAugrf_lbugrfmsrqcpmjmega @H, BgeBg/q7Q7/23g/ 6U/1,

7 A_aagMmj_jGgaQglsm_Rpcgrm_jE, MUasjr fcr _rgrgq@tgpsqgldcargmlgln_rgc

Establishment and evaluation of a hypersensitivity method of real time fluorescent PCR for hepatitis B virus detection

VGA Oiao JGAO Jili DONE XhiqiangWANE Honghui HGANE Viwen

Research Center of Kedical and Pharmaceutical Bioengineering, Kinstry of Health National and Regional Hoint Engineering Jaboratory for Clinical Kedical Kolecular Diagnostics, Euangdong Province Nucleic Acid Kolecular Diagnostics Engineering Technology Research Center, Euangdong ProvincialClinical Kedical Kolecular Diagnostics Engineering Technology Center, DAAN Eene Co , Jtd , Of Sun Wenetsen Sniversity Euangzhou Euangdong China 510445

ABSTRACT Obhective TaqŲman real Ų time fluorescent PCR was used to establish a method for hypersensitivity detection of hepatitis B virus DNA HBV DNA load hereinafter referred to as a hypersensitivity reagent and its clinical application was evaluatde, Kethods Based on the analysis of the HBV DNA genome sequence in EeneBank a pair of specific primers and probes were designed in the S and C regions of HBV viral genome using Prime5 , 0software and the reaction system and reaction conditions were optimized by TaqŲman probe technique Results The established HBV DNA hypersensitivity detection method has a sensitivity of10 GS - mJa linear range of20 to 1 Â10⁷ GS - mJand an accuracy of100 # , The coverage types are A B C D E F and H , The intra Ų and inter Ų assay coefficient of variation between batches is within5 # , The results of75 clinical samples showed that compared with a domestic reagent the

RUÂlSÂ‡jÚ°ÞÞ7$#GrÊÇr ±ë ‘4ÊÐÝU—@W$ÇívÇ8dÞ±Þ×3±'‡S°Å_# d€ ð *S±Ð Q9µ &5†5† X@5ô3I F Q TsXjÚr_

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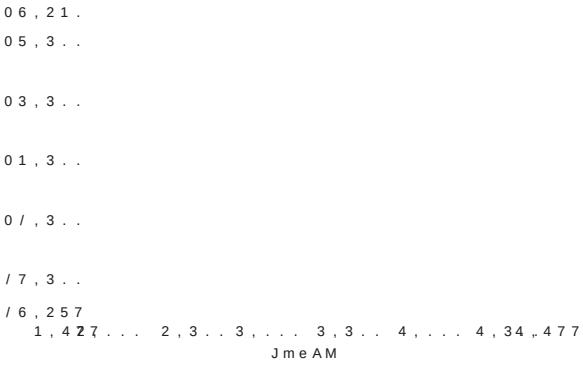

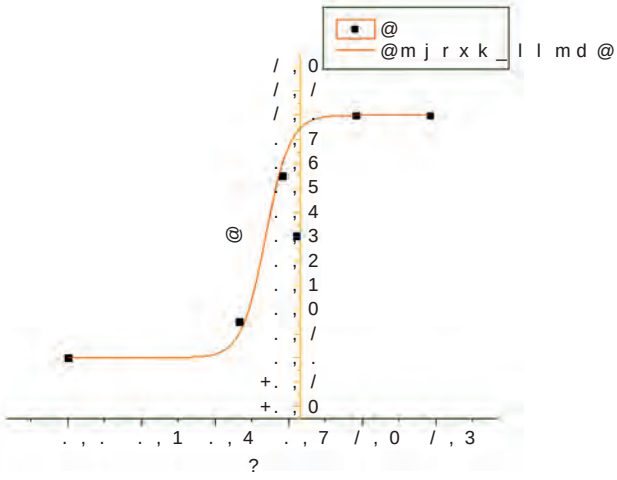

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Dge/sp Rcf c pcqsjrqmdos_lrgr_r

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Dge3pQc lqgrgtgrwbcrcpkgl_rgmlrcq

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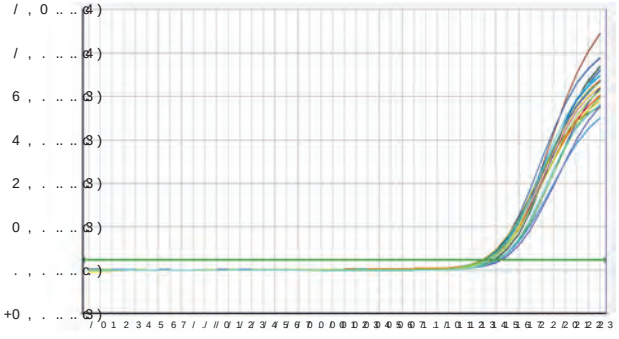
ج e ε 15.41 GS-kJ Ḥ ӈ

ε 2. GS-kJ ه 3ɟ



1

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bcrcargmljgkgr

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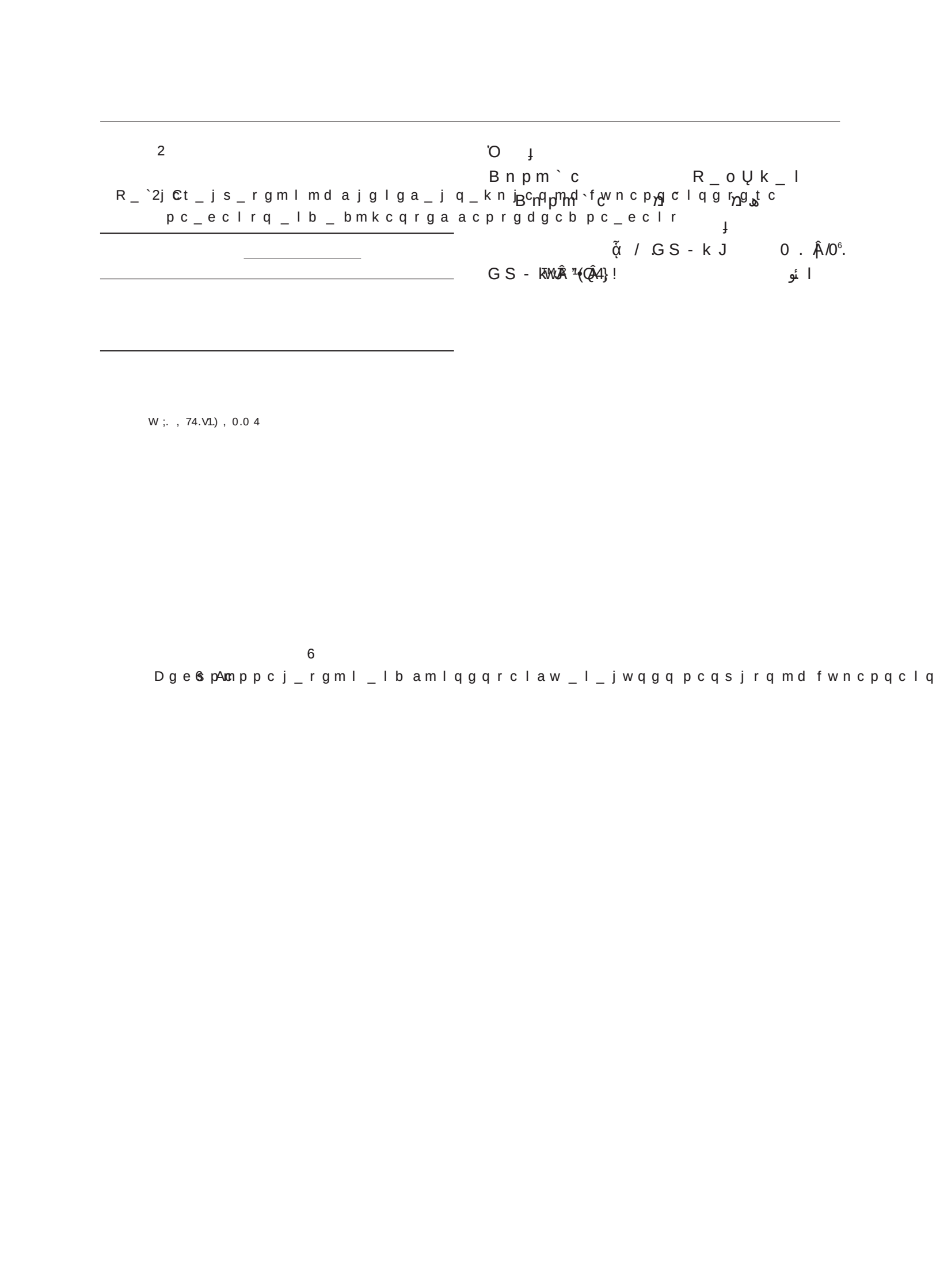

The application value of high sensitivity HBV nucleic acid test in preoperative screening

JG Baoqi[2] CHEN Peisong[1] HSANE Hao[1] WS Vuegao[1] HSANE Bin[1p]

1, Department of Jaboratory Kedicine The First Affiliated Hospital Sun Wat Ų sen Sniversity Euangzhou Euangdong China 510080 2, I ing Ked School of Jaboratory Kedicine Euangzhou Kedical Sniversity Euangzhou Euangdong China 510180

ABSTRACT Ob h ective To explore the application value of high Ų sensitivity Hepatitis B virus HBV nucleic acid detection in preoperative screening Ķ ethods Serum samples were collected before surgery and HBV DNA and HBsAg in serum were detected by high Ų sensitivity fluorescence quantitative PCR high Ų sensitivity PCR and chemiluminescent microparticle immunoassay CKGA , Specimens with inconsistent results from both methods were tested for HBV DNA using the Roche Cobas AmpliPrep - Cobas Taq Kan automated nucleic acid detection system Ŗ esults Among 517 serum samples 70 cases 15 , 3 # of HBsAg Ų positive specimens were divided into groups according to the quantitative results of HBsAg group

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BLA Ý τ

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@/	7.746,4.	:/.	:0.
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A/	17445,/4	:/.	:0.
A/	3341,2.	:/.	:0.
B3	4 03,/6	:/.	:0.
B4	.34.,3/	:/.	:0.
B4	5 /73,02	:/.	:0.
B4	7 14.,31	:/.	:0.
B5	5 756,0/	:/.	:0.
B5	6 /50.,74	:/.	:0.
B6	.21/,54	:/.	:0.
B4	2 .,..	53,42	0/,5
B6	3 .,..	/2,.3	/54

1 / 3

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FBcA` ҭ FBaA` 1 ҙ ε FBqAe ҡ FBcAe ҡ

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BLA FBqAe FBT BLA Њ

ң щ ε 4 ј

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7 5 6 ,G6S/ - kJ / F@q?e ε /

5 0 . G 5 4 kJ ε F@q?Fe@c?Fe@c?`

F@a?` ɟ NAP ج ᾷ / 1 { »P |

Comparative study of high sensitivity and conventional fluorescence quantitative PCR in the monitoring of antiviral efficacy in patients with chronic hepatitis B

JS Hianhua WANE Ji X HAO X haoxia JG Oianlin JG Kinran JGS Wuzhen DAG Erhei CHEN V iuli
Department of Jaboratory K edicine the Fifth Hospital of Shi h iazhuang Shi h iazhuang Hebei China 050021

ABSTRACT Ob h ective To compare the difference between high sensitivity and conventional fluorescence quantitative PCR in the monitoring of antiviral efficacy in patients with chronic hepatitis B CHB , K ethods A total of 1 2 1 samples of 2 7 patients with CHB were negative :500 GS - mJ specimens with common PCR and were reviewed with high Q sensitivity PCR reagents Results Based on the quantitative results of serum HBV DNA using high Q sensitivity PCR 1 2 1 negative samples with common PCR results existed in the following five conditions namely <500 GS - mJ 20 | 500 GS - mJ 10 | 20 GS - mJ :10 GS - and negative , The proportions were 5 # 31 , 7 # 18 , 2 # 30 , 5 # and 5 , 5 # respectively , U ith the gradual increase of serum HBV DNA level the level of AJT AST levels and abnormal elevated rates in each group also showed a gradually increasing trend , However only the AST levels of each group were significantly different

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1.1 m

49 ϛ è CFB ϫ ε 2.17 1 2.19
6 ϯ A ├ ɟ Ấ ỖA
ε 18 ϟ ẇ w ɔ ậ ‴ FBqAe
6 Y ɔ ỽ ă FBcAe CFB
ɟ ỖA ´ ẹ ђ ϖж ӧ
FGT ´ ӧ
ẹ ђ Ɗ ẻ ɔ
Ɗ ґ ˝ t ´ ẹ
ђ O ậ ϯ ϧ Ά ẹ í
ɟ Ъ A ├
Ң ϟ Ж ϫ Ъ ˛ Ш ɟ

1.2

ϫ ´ ћ ϕ ی ≟
2.15 ђ[1] Ψ ɟ
▌ Z Ậ ắ
˘ ..5 ke m ɟ

1.3

ậ ϯ ϖ ˜ 4 ϖ12 ϖ24 ϖ36 ϖ
48 ϟ FBT ϟ FBT BLA

Γ ϯ Aj_ lglc _kglmrp_ lqdcdp
_qc AJR ϖ ũ ϯ Aqn_prga _kgp
lmrp_ lqdcp_ qcAQR ɟ NCP Ң 141
oy NCP FBT BLA
:5. . G S - k J ɟ
1.3.1 ζ Ѧ ɔ Ά Ң
BA32. . ẫ ϩ Ѧ Ψ
ϯ ė oy ắ ˘ ABG75. . ی ẉ NCP
Ѧ ѧ J gdc Rcaf lmjmegcậ ˘ ң
ѧ Cnnc lbmpdắ ˘ FBT BLA
Ң Ψ ϯ ė oy ắ ˘ ẹ
Ш ε 5. . G S - k J م ε
5. . | 5.Â1.[8] G S - ɟk FBT BLA Ң
Ψ ϯ ė oy ắ ˘ ẹ Ш
ε 2. G S - k J م ε 2. | 1.Â1.[9]
G S - ɟk_Jsrmjs k m A2. . . njsq ی ẫ ɔ ґ ẉ
Ѧ ѫ oy ắ ˘ ɟ
F76. . ی ẫ ɔ ũ Ѧ ắ ˘ ɟ
1.3.2 FBT BLA
ẉ NCP FBT BLA
˜ ɟ
1.3.3 FBT
ɔ ґ ẉ ӧ ũ
FBqAe ϖ Ų FBϖ FBcAe ϖ Ų FBϖ Ų FBa ɟ
1.3.4 ˙
ẫ ɔ ũ Ѧ AJ RϖAQR
ɟ
1.4
í Ấ Cvacj Ψ
QNQQ17. . Θ ũ
w $\bar{x} \pm s$

2

2.1 NCP Ά NCP CFB
FBT BLA
141 oy NCP CFB
Ψ NCP Ң
FBT BLA G S - k Jϯ w ; 5
◗ ≤5. . ϖ2. | 5. ϖ1. | 2 ϖ :1. G S - k J
ϫ ũ ậ ε 13.5 # ϖ31.9 # ϖ18.4 # ϖ3. .5 # ϟ 5.7 #
1 ɟ

/ N A P N A P A F@ F@T B L ?

2.2 CFB FBT BLA Ά A J R@AQR Ą̆

NCP Ḥ FBT BLA

ŭ̃ ˘ A J R@AQR Ỹ 2 ɟ

FBT BLA ˘ A J R \ ╕

† ӂ τ

0 A F@ F@T B L ?? J R? Q R

$\bar{x} \pm s$

Table 2 Relationship between serum HBV DNA an ALT an AST in CHB patients $\bar{x} \pm s$

F@T B L ? G S - k J	? J R S - k J	? Q R S - k J
	╕	╕
<3 . .	/ 7 6 2 0 , 2 1 ,13/ §,42 1 / , 4 1 5 ,/ 26 §, 1	
0 . | 3 . .	2 3 / .0 0 , 0 0 7 ,/ .3 §,77 0 . , 1 . §,/ 5 3 , 6	
/ . | 0 .	0 4 4 0 1 , 0 4 ,/ 3 0 §, 0 5 , 5 0 6 ,60, §/	
: / .	2 1 2 7 , 1 1 . ,0 4 7 §,43 / 1 , 0 7 6 ,/ /. §, 6	
	6 / / 0 , 3 0 3 ,7 3, §5 . . 0 0 ,16, §5	

<3 . G S - k J

2.3 CFB FBT BLA Ά FBT Ą̆

FBT BLA н ˘

FBcAe ⁄ ς ŭ̃ н † ɟ ẹ

Ψ FBT BLA FBcAe н

Ħ 1 . \| 2 . G S - k J 5 . . G S - k J τ

1 A F@ F@T B L ? F@c ? e Ụ F@a

$\bar{x} \pm s$

Table 3 Relationship between serum HBV DNA loa an HBeAg an anti hbc status in CHB patients $\bar{x} \pm s$

HBV DNA IU ml		
500		
20 500		
10 20		
10		

3

ǻ ˘

N A P Ụ

/ 2 oy F@T

: 3 . G S - k J A F@

N A P c 6 oy

3 , 5 ε# ɟ F@T Y

k P L ? ï

ц

ε / \|Â 1 / U3 .- l r 4 -ɟ F@T ħ B L ?

2 Y P L ? / \| Y 0

ɟ N A P Q A ˥

˥ ’

/ 0 / / 1ρ

ٹ ң F@T BL?/..GS-kϕJیی Ặ
FAA ϕیی F@T BL? ϕیی Ặ
í ɟ ≠ ﷺ ך 0./40 0./6/.ﺋﻮ ← ɕж ├
ﾉЧ F@T BL? /..GS-kJ74ą FAA
F@T BL? ŭ ẍ в ˙ A F@T BL? Ặ ﾉí
τɟ بم 74ą ϕیی Ặ FAA Ψ F@T BL? /GS-kJ52ą 55,/ɟ#
F@T BL? /GS-kJ ɔ ח в ˙ ?JBCUER ﾈ F@T BL?
/GS-kJ ɟ ϕیی Ặ FAAA ϕیی "A Ặ F@T
BL? F@T BL? í τɟ
Ψ ϕیی ң F@T BL?

Clinical value of high sensitive HBV DNA detection in hepatitis B related hepatocellular carcinoma

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ABSTRACT Obhective To investigate the relationship between hepatitis B virus serum high Ų sensitivity HBV DNA detection and hepatocellular carcinomaHCC by detecting low Ų viral HBV DNA: 1 000 GS-mJin patients with hepatitis B Ų associated hepatocellular carcinomaHCC, Kethods From February2014 to October2018 74 patients with HCC who had HBV DNA levels of less than1000 GS-mJ in the general outpatient and inpatient hospitals of the Third PeopleBHospital of Hubei Province affiliated to Hianghan Sniversity were selected, Serum high Ų sensitivity HBV DNA was detected to analyze the correlation and clinical significance of serum immunological markersliver function markers and HBV DNA leve, Results Of the74 patients with hepatitis B Ų related HCC 2255, 1Had HBV DNA levels greater than10 GS-mJ, The incidence of cirrhosis and liver functionTT ČŲET in patients with HBV DNA levels greater than10 GS-mJ were higher than those with HBV DNA levels less than10GS-mJ,Conclusion HBV Ų related HCC is associated with the continuous replication of hepatitis B virus, High Ų sensitive HBV DNA detection is more clinically significance than HBV DNA detection by common fluorescent probe methods,

IEW UORDS Hepatitis B virus Jow serum hepatitis B virus DNA level Hepatocellular carcinoma HighŲsensitive HBV DNA detection

1

1.1 í

├ Ӈ ᛘ Ӝ ̃Ā ̓ ┐ 2.16 2

2.18 1. ئۆ ← є ж

├ ᛘ Ч 96 ҳ ф ی Ă pU‘ s& pU•

FCC ẉ FBT

BLA :1 . . . G S - k ф Ψ 81 ҳ 15 ҳ

28 | 76 ج 51.4§23.6 ɟ FCC ẇ ẇ ɔ̄ k̄ ɔ̄

χ

] h'6 `

0 F@T B L ?

R _ `0j N r g c l r q u g r f q c p s k f g e f q c l q g r g t g r w F@T B L ?
j c t c j q _ p c _ q q m a g _ r c b u g r f a g p p f m q g q „ _ l b _ l r g t g p _ j r p c _ r k c l r

		F@T B L ?	F@T B L ?
ą̈			
ɔ F@T	1 4	/ 7/ 7 , 6	/ 5/ 5 , 5
ɔ F@T	4 .	3 33 5 , 1	3 3 , 0
	5 1	4 14 3 , 4	/ ./ . , 2
	0 1	/ // / , 3	/ 0/ 0 , 3

χ 2

R• X '0 € R• X 9 •Ec FxĐ @ p

3

F@T ƒ
F@T B L ? ε ó ζ ′
ˆ Ό F@T B L ? щ
F@T
B L ? N A P ; ε / . . G S - k J
Y ; F@T B L̈ ?
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ó ı ą̃ O
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F A A F@T B L ?
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F@T B L ? ɟ F@T
B L ?
ó ɟ
Ж CQ ? J F@T N A P
; ; / GS - k J ' ą̃
ɟ / / F@T B L ?
˥ F@T
w Ҡ Ӗ F A A
/ 0 Ụ / 2 ɟ
F@c ? e ex F@T
F@c ? e F@T B L ? Ė
F@T B L ?
F@c ? e ζ ε
ئى

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2.19 3 2.19 7 ئۆ

18. ʒ FBcAe FBT ε

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ϕ يى ج ɦ2.15 ϕ يى

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Ψ Ȯ ɞ ẹ Ψ 11. ʒ

7. ʒ 21 | 9. ج 47.92§13.42 ɟ

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1.2.1 ʒ Á NCP א l

ʒ ɔ Ḥ BA622 Ψ

غ نح oy ǎ ˘ 96 Ψ Ẩ

4 J Ỉ ɞ2. J Ŏ Ã Ů Ŏ J Ỉ

/ 0 F@T BL? GS-kJ

R_`/jBcrcpkgl_rgml md F@TcBlerSpcqsjrq`w

0 0 F@T B L ?

3

χ^2

2 2

1 0 F@T B L ?

NAP F@T BLĖ?

NAP F@T B L ?

F@T B L ?

F@T B L ?

F@T B L ?

/ 6 . F@c ? e

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ث ه У NAP Ḥ ~ ه У Ḥ Ȧ i ~ i Ḥ

ϕ يى F@TBL? ɟ ﻟﻪ ﻳ ɟ i Ḥ ɿ 3 /o2 ϕ يى

ه У ã ɿ Ȧ ɿ NAP Ḥ F@T BL? w ǔ

ه У Ḥ Ỹ ɿ Ȧ i Ḥ ɿ Ặ ɟ بم i Ḥ ɿ ه У Ḥ Ȯ

ǔ ǫ ε 5 5 , 1 5 6 , 3 # ´ ǔ ǫ ε 5 , 0 6 , 4 # Q n c _ p k Ặ_ǔ l Ξ

Ḥ F@T BL ? 0 . | // , 6 5 Ŝ - k J Ỉ Ặ

Clinical comparative study of two quantitative methods for HBV DNA detection

UANE Shuang ESO Hie UANE Dagang SHG Hingren PAN Keichen WGN Shangqi HE Chaonan KENE Huan XHANE Viang UANE Wa h ie

Clinical Jaboratory Bei h ing Ditan Hospital Capital Kedical Sniversity Bei h ing China 100015

ABSTRACT Ob h ective To compare the results of a domestic real Ụ time fluorescent quantitative PCR of & Domestic reagent ' with a imported reagent & Gmported reagtent ' for detection of hepatitis B virus HBV DNA , Kethods A total of 51 2 plasma samples of chronic hepatitis B were collected according to the results of imported reagent test , HBV DNA was quantitatively detected by domestic automatic nucleic acid extractor and PCR high sensitive reagent in parallel to analyze the difference and correlation between the results of imported and domestic reagents , Results The positive detection rates of imported and domestic reagents were 5 5 , 2 # and 5 8 , 5 # and the non Ụ conformity rates were 5 , 2 # and 8 , 4 # respectively , There was no significant difference between the 2 reagents , Spearman correlation analysis showed that the correlation coefficient

ãã O ǎ Ǎ ►

f c n _ r g r g F@@ t g p s q

φ ãã 0 , ã 5

ж 6 6 , ã 0 3 #

/ ɟ ئى F@T

A f p m l g a f ã F@r g r g q @

φ 0 ɟ F@T B L ? ζ

ó F@T F@T B L ? ǎ ‿ Ǎ ڑ ە ABG75.. ىي ẉ

Ƙ 1 ɟ F@T B L ?א

F@T ’

ó Ė

2 ɟ

N A P F@T B LĖ?

3 ɟ F@T B L ?

N A P φ

4Ц.Б ɟ ɟ F@T

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F@T

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1.1

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← Ш ئى ﺝ ├ Ẇ Ч ф ىي

514 ʒ ˜A ´ ĥ ф

ىي ≟ 2.15 ĥ ɟ ﺝ ε

Ⱶ m FBT ẹ ĥ Ɗ ɇ

ʾ в ﺍ ɟ

ﺝ ʾ Ш ɟ

/ 0

R _ `/j Ǻ f _ p _ a r c p g x _ r g p m d _ a e m c k l n r _ q p g q m l m d

1.2 ζ Ḥ ﺍ Ǻ ڑ

CMBAQ AkỤ

nj Np cn ך Ǻ ε 6.. J ﻫ Ḥ ε

CMBAQ FBT Rcqr t2.. Pmafc ɟ ە У FBT

Qk_pr32 ã ך Ǻ

ε 2.. J ﻫ Ḥ

NCP ﻫ Ḥ ە У Ψ نح غ oy

ە ABG75.. ىي ẉ

1.3

514 ʒ ỗ ợ i ﺍ ە У Ḥ

Ḥ Ш ˜A ɟ 2

FBT نح Ɗ m ﺝ ẉ

NCP ф ж Ψ FBT

ɟ 2 Ḥ 1

ɟ

1.4

Cvacj e FBT

BLA jme1.

QNQQ16.. Ɵ ỗ ɟ

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2

2.1 2 Ḥ

Ǎ ф 514 ʒ ɟ i

Ḥ e ỗ ε ł ợ FBT Ń

117 ʒ :2. G S - k J 11. ʒ 2. | 1<7Â

1.8 G S - ₭ J 287 ʒ ẹ Ψ <1.7Â1.8 G S - k J

33 ʒ ɟ ە У Ḥ Ȧ i

ỗ 2 i Ḥ

Ȯ ε 77.2 # 3975514 ە У Ḥ

Ό ε 5 6 , 32 # 32 /- 2 0

Ό

0 0

R _ `0jAcm k n _ p g q m l m d0 p f c _ e p c c l q r s q j r q m d

2.2 ه У 1 i Ή Ặ 1m ه 1 ɟ Ξ Ή Ặ p ;..966

ὗ N:.....1 J Ẻ Ặ ه

ه У Ή 1 i Ή Ψ 285 ʒ 1A Bj_l b Ų Ajr k_ ὗ Ξ

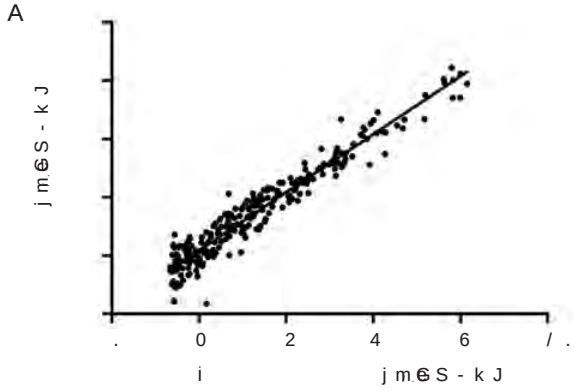
Ҥ ; e ẹ Ψ 33 ʒ <1.7Â1.8 G S - ὗ ه У Á i Ή e e ج

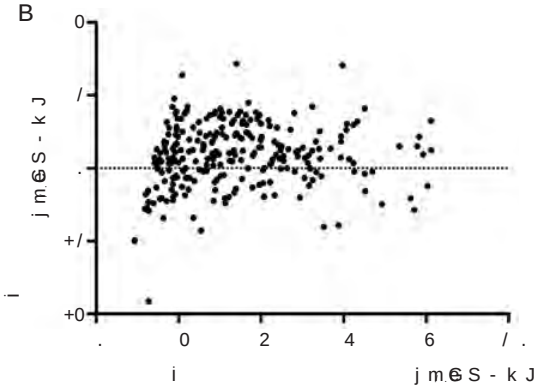
k J ʔ ε <8.23 33 ʒ e ε ..173jme. G S - k95J # ' ɲ ┘ ε +..6779 |

Ή e ε 8.55§..39 m 1..24 . jme1. G S - ɟk95.6 # 241252

ɟ ʒ 2. | 1.Â1.8 G S - k J Ỉ e ʒ 95 # ' ɲ ┘ Ỉ ه У Á i Ή Ẻ

252 ʒ e ʔ ~ Ặ 1m ὗ m ه 1B ɟ





/ 0

D g e s p f c c A m p p c j _ r g m l _ l b a m l 0 p g q _ r e c d a w q _ l _ j w q g q ` c r u c c l

ʔ ┘ Ή Ψ

Ặ ὗ ه У Ή Á i Ή ˘

Ặ ج ʔ ┘ م Ỉ Ặ

ᾷ ه У Ή Á i

Ή ʒ ʔ ж FBT BLA F@T &G S - k J '

Ὼ ɔ m 3 ɟ ẹ Ψ ʒ Ή ┘

2. | 13.G S - ɟ Ẻ Ặ Ή

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3

ʔ ɟ K F@T

F@T B L ? ε ó K Ẻ

ó w ɟ i Ẻ

UÀ @ €OŽEÄ¤ÂÞEC U5%EG %.™ÆÞ8'3 ÿ3TŽÿŸ ð&'

UÊÂÕ ÿ9Bÿ7=ÕÒ Y=ÙÀÞ F @Úÿ2 ÞÀÞÚÁ ÕÕUŸ

1.5

2 ὲ ⅃ φ

46 ϡ 1 ` ى Γ ى ᾤ ᾠ

2 ⅃ ɑ4 ⅃ ɑ12 ⅃ ~ 2 ε

ϡ ὗ ⅃

1.6

ج QNQQ2 . . . Θ

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e p m s n _ l b r f c b p s e u g r f b p _ u _ j e p m s n

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ε Ǎ F A T

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F A T P L ? ж

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22 ج 44.68 ؤ 12.96 ؤ

1.2

oy ʾ ƒ i ʿḤ ʅ ه У ʿḤ

Ə O Ш Ψ Ã

ؤ 2 ؤ Ɗ ɔ ح m ج

ʔ ʅ ɔ ج ه R_oŲ

k_l ẉ ´ ه Ψ FCT

ؤ 8 ؤ 1.5 k J

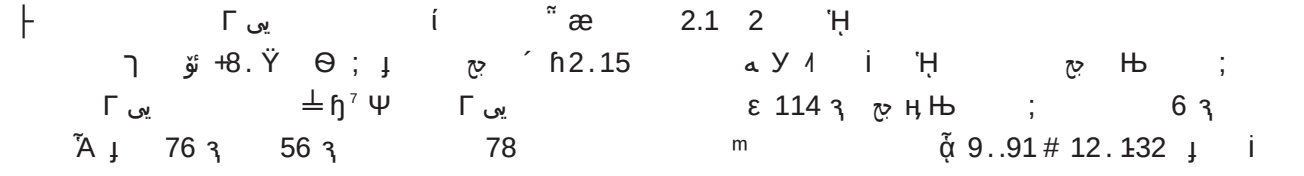
ʔ ɔ ʿḤ

ʔ ъ ʿḤ Ψ ʔ ʿO FCT א ɔ

~ ₱ ʒ ʿẠ א φ ~ 2. J

ʿẠ א ʊ̃ ɑ̃ NCP Ψ ɔ FCT א Ψ

ʅ ق̃ ʊ̃ ɑ̈ Ã ʔ ~ ɞ



FCT ɨ ɞFCT ɨ ɞFCT í

ɨ ʅ FCT ל ɨ 4. J ؤ

8 . . . pnk ~ ه ⌟

ه ؤ 2 ʿḤ ל 1 ؤ

1.3

Ep_nfn_b ƒ P 3.6. . ʊ̃ ש

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├ Γ ی í ˜ æ

ʔ ئو +8. Ÿ Θ ; ؤ ج ´ ɦ 2.15

Γ ی ⊥ ɦ 7 Ψ Γ ی

Ã ؤ 76 ʒ 56 ʒ 78

2

2.1 2 ʿḤ

ه У ʅ i ʿḤ ج Ҥ ;

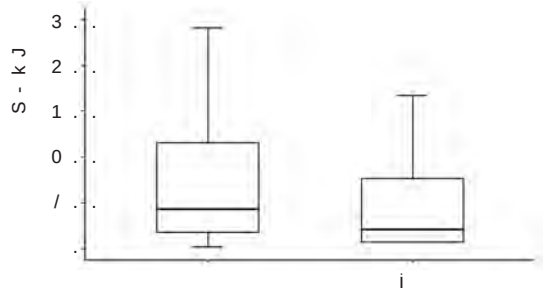
ε 114 ʒ ج ɦ Ҥ ; 6 ʒ

m ɑ̃ 9. .91 # 12. 132 ؤ i

/ 0

R _ `/j ɑ m k n _ p g q m l m d n _ p _0 p c r _ e p c b r _ q _ ` c r u c c l

ʿḤ	ʔ	ه		J	م G S - k J	; G S - k J
ه У	Q k _ p 32	ABG 75. .	5 ū SRP	2. .	5. | 11 Â 8	2.
i	Asrm k _rcb Cm`_q A k nj g Npcn	Cm`_q R_o K_l	5 ū SRP	65.	15 | 11 Â 8	15



2.2 2 ʼḤ ǖ

ɑ У ʅ i ʼḤ ʒ Ҥ ; 114

ʒ ʒ FCT ǖ ǟ ε 2.38Â

1.4 | 5.6Â1.6 G S - k J5.47Â1.6 | 1.39Â1.7 G S - k J

:/ . . G S - k J

1 0 F A T

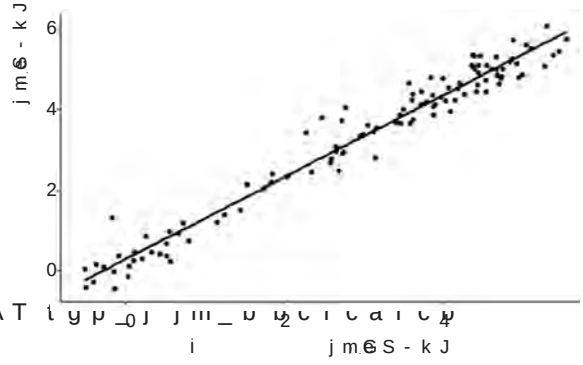
D g e s p A c m k n _ p _ r g t c _ l _ j w q g q m d F A T t g p

` w 0 p c _ e c l r q

2.3 2 ʼḤ m ǖ

2 ʒ Ҥ ; 114 Y

e ʅ ~ Ặ ǖ Ặ



/ 0 F A T

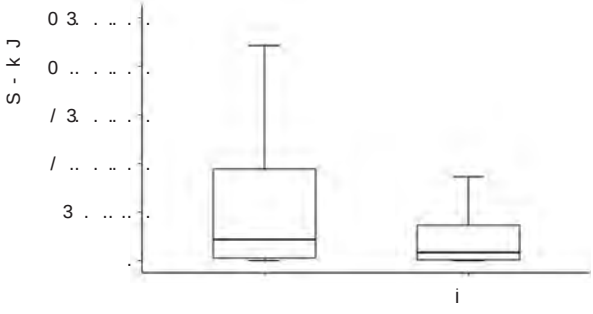
D g e s p A c m k n _ p _ r g t c _ l _ j w q g q m d F A T t g p _ j j m _ b b c r c a r c p

` w 0 p c _ e c l r q

2 0 F A T

D g e s p A c m k n _ p _ r g t c _ l _ j w q g q m d F A T t g p

` w 0 p c _ e c l r q



</ . . G S - k J

0 0 F A T

D g e s p A c m k n _ p _ r g t c _ l _ j w q g q m d F A T t g p _ j j m _ b b c r c a r c p

` w 0 p c _ e c l r q

3 0 F A T

D g e s p A c m l q g q r c a w _ l _ j w q g q m d F A T t g p

` w 0 p c _ e c l r q

3

F A T P L ? Γ Ė

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ث φ يى c Ɗ F@c ?Ae Ų F@Fc@c ?Ǹ φ يى í
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0 . ʒ3 1 F@c ?ɞe Ų F@Fc@T B L ? ǖ Ỹ ˘ ' ɞ? D N
ʒ ɟ بم ǹ 4 6 , . # F@c ?ʒe/ | / A M,Ɗ . , 6 # </ . .A,M.ƆA c Ɗ
τ

Clinical characteristics of chronic hepatitis B patients with both HBeAg and HBeAb positive

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ABSTRACT Ob h ective To investigate the clinical features of hepatitis B e antigen HBeAg and anti Ų HBe HBeAb double positive chronic hepatitis B patients , Kethods 500 patients with chronic hepatitis B from Hanuary 2014 to December 201 5 were selected as sub h ects 122 cases in group of both positive 1 5 3 cases in group of HBeAg positive 205 cases in group of HBeAb positive , The distribution of HBeAg HBeAb and HBV DNA copies in the three groups was compared , The abnormal liver function index and AFP results were evaluated , Results Gn the double positive group 48 , 0 # of patients had HBeAg 1 of 10 , COG and only 0 , 8 # of patients had 10 < 0 COG which was significantly different from the e antigen positive group

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CMG31.1 # ε 1 | 1...CMG ..8 #

ε <1....CMGÁ c Ɗ

τ

/ c F@c ? e

χ^2

2.2 אָ Á c l Ų FBc ὗ

אָ 63.9 # Ų FBc ε | 1..

CMG23.8 # ε | ..5CMG 12.3 # ε

. | ..1CMGÁ c Ɗ

τ

0 c Ų F@c

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2.3 3 FBT BLA

אָ 64.8 # FBT BLA ʼɡ

5.. | Â1.7 - k J3..3 # :5Â1.2 - k J

4.9 # ≤1Â1.7 - k Jc Ɗ 18.9 # ≤1Â1.7

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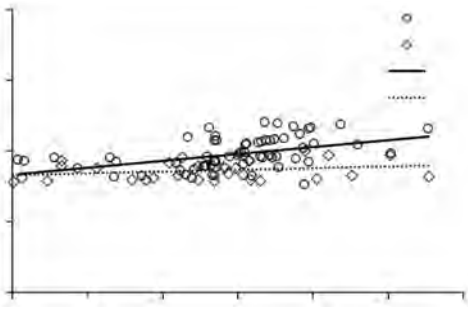

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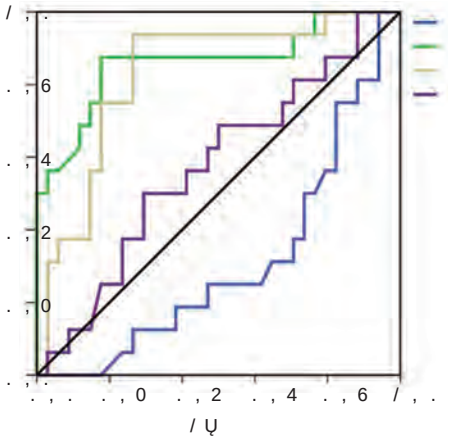

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R ? A C ϕ D ɟ ~ ı Ч ϋ ε

The clinical effect and immune function of anti HBV on recurrence and metastasis of liver cancer after transarterial chemoembolization

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ABSTRACT Ob h ective To investigate the clinical effects and immune function of antiviral therapy in patients with hepatitis B virus Ų related liver cancer receiving transarterial chemoembolization TACE , Kethods 84 patients with HBsAg positive liver cancer treated in our department from Hanuary 2015 to February 201 5 were selected and all patients were treated with TACE , According to the application of nucleoside acid analogues in antiviral treatmentthey were divided into experimental group

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ε 54.5 # 18 33 Ξ

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1.4

QNQQ21.. ǔ

$\bar{x} \pm s$

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2

2.1 2 ˜ Ỹ

ε 79.8 # 37 53

1 0 $\bar{x} \pm s$

R _ `1j A m k n _ p g q m l m d g k k s l c 0 desp l m a s r n g q m l ` c r u c c l r f c

Ì ǫ̈ -

2.3 2 ϕ Ỹ

ǫ̈ 2 FBT BLA ẅ FBqAe

τ

2.4 2 ' Ỹ

2 ئۆ ǫ̈ A J RɞAQR ɞE E R

τ

χ^2

2.2 2 ẍ ' Ỹ

ǫ̈ 2 CB3) ɞL l ɞCB4) - CB8) ʒ

τ

2 0

3 0 $\bar{x} \pm s$ U L

Table 5 Comparison of li er function between the 2 groups $\bar{x} \pm s$ U L

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F@T /1 ɟ ’

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F@T B L ? c τ ế

ζ φ ς ε ɟ

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̀Y ’ w /2 ʍA ς

ṇ F@T F@T 7 ɟ ɟ 0 /Y

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A B2) - A6B; ˧ ɔ L I

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R ? A C

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B L ?) F@q ?)e ɟ

R ? A C

ƒ F L T ɟ ε

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Ḥ Ψ غ نج oy ắ ˘ Z̲
ж DA K 83A ɞ Baj Ụ2 ɞ B_v l ج ه A`a_k
ắ ˘ ẽ H Ḥ ه BB ắ ˘ אָ
ẉ ˆ ا غ نج Ḥ ẹ ש غ نج
ج ه Npm k ce_ắ ˘ k g P Ụ3182 k g k g aq ש
k g P Ụ L ɞ

1.2

1.2.1 ש ỗ
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K G 164 . نج Ế نج NBQ 3 Â5 k g l
24 f m نج Ế Ẩ 37 Ÿ ɞ l ỗ 5 # CM̲
نج Ế نج Ế ɟ ך K FCC 97F
Ҥ 96 1 Â1 . 5 Y - Ẩ 37 Ÿ
نج Ế Ỉ نج Ế 4 f ´ ậ 6 . # Ụ
7 . # k g P Ụ3182 k g k g aq Á k g P Ụ L ỗ ậ
K FCC 97F ỗ ậ ε k g P Ụ3182 ɞ k g P Ụ
L C

1.2.2 o PR Ụ NCP k g P Ụ3182 ɞ

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1.1 Á ζ Ḥ
K FCC 97F ɞ F s f7 ɞ K FCC J K3 Á
RF J C 2Ụ ج ه ARCC
ɟ PN K G 164 . نج Ế نج Á ج ه
E g`am ắ ˘ Rp g x m j Ḥ Á J g n m d car_k g l2c . . . pcỤ

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ẇ ɟ
1.2.4 ἕ H
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ɔ Hь 6 NBQ
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Ⱥ ἕ H Ỹ ɟ
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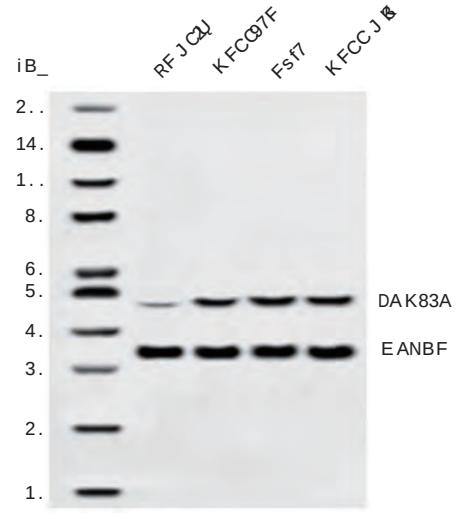

/ D ? k6 1 ?
D g e ś pCcv n p c q q g ɷ6 1 ?m d pDm? Kc g l

/ k g Ɛ Ụ 6 OD ? k6 1 ?
$\bar{x} \pm s$

$\bar{x} \pm s$

R F J C Ụ
K F A Ⱥ 5 F
F s 5f
K F A A J1K

2.2 kgPQ3182 ˜ DAK83A
qr_pB_qc ɲ ɲ kgPQ3182 Ά
DAK83A 3ū SRP ğ ´ Ḥ ь 2A ɟ Ẋ
ẇ Ỉ ż Ấ
DAK83A 3ū SRP ẇ Ỉ ż I Ά

k g P1 Ų 6 k0 g k g a q ;

0 $\bar{x} \pm s$

$\bar{x} \pm s$

A B

A DA K83A 3 ū SRP Ψ Ά k g P Ų 3182 Ў Ώ

B DA K83A

A Rfc 3 ū SRP md DA K83A am l r_g l q _ l sajcmrgbc qcosc l ac am k Ų hjc

k c l r_pw rm k g P Ų 3182 B rfc cvnpcqqgm l md DA K83A npmrcg l

0 k g P1 Ų 6 0 D ? K6 1 ?

D g e 6 s pkcg P1 Ų 6 r 0_ p e c r q r f c p c e s j _ r g m l m d

D ? K6 1 ? c v n p c q q g m l

2.3 k g P Ų 3182 K FCC97F

ἕ H ⁄ ἵ

oPR Ų NCP K FCC97F Ψ

k g P Ų 3182 k g k g aq k g P Ų

3182 Ψ k g P Ų 3182 ╗

3 D?K61? KFAA5F $\bar{x} \pm s$

$\bar{x} \pm s$

4 D?K61? kgPU60 KFAA5F $\bar{x} \pm s$

$\bar{x} \pm s$

1

1.1 ʒ

ʔ 2.17 6 2.19 6 Ҥ Ҝ

FBT 75 ʒ ε ʒ

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ϕ ىٮ ≟ 2.15 ŋ[8] Ψ Ặ Ҥ ϕ

ىٮ ʾA ɟ ├ Ӈ

ʅ Ж Ҷ ʾA Ấ ʒ ѡ ҕ

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1.2

1.2.1 ŭ

˚ ϕ ىٮ Ӧ ŭ ʾA[8] 75 ʒ

FBT ŭ ε GR 2. ʒ FBcAe) в

AJR6. S - вFBT BLA<1.[5] - k JвGC 3. ʒ

FBcAe) - вAJR6. S - вFBT BLA<1.[5] -

k J вGA 25 ʒ FBcAe + вAJR6. S - вFBT

BLA :1.[5] - k Jˀ 25 ʒ ϕ ˊ

ɾ ε ɾ ɟ ǫ̈ ǫ̈

ʒ в ҕ т Ė ˈ ɟ

ɔ 1.. ʒ Ɔ FBT BLA ˟

ˀ ŭ ε ӈ FBT BLA :1.[5] - k Jв

Ψ 1.[5] - k ĴFBT BLA :1.[6] -

k JT@5 $BJ

Z* вЕ вĮDЎ₩Ғ5 Ѧ₩ĝ=2₦ÕЎ3₦ѦX•ÓЖ2#,Ю5'ЯЕРЂ ``ÜQ@

1.2.4

3. ʒ GC 1

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Ǻ F2.1..141 Ḥ ε 5 ke-ɓ 12 Y

˜ Ố A J Rɞ ɿ ɛ̇

Ά ǿ ǖ

1.2.5 ǖ

QNQQ13.. Θ Ḃ ǖ

ɯ $\bar{x} \pm s$ *t*

Graph

Pa Prism7

2

2.1 ɿ FBT BLA Ά ɛ̇ Ặ

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ˆ FBT BLA ǖ Ẻ I ǖ

1.3 ǖ ˆ FBT BLA FBT

ɿ ɛ̇ 1 ɟ

ъ ą̃ G 4 ɥG 5 Ų ɔ ɔ

† ɔ ╗ ╗ ẹ

ʕ ╗ 2 Y ą̈ ε

2.2 A J R Ά ɛ̇ Ặ

A J R ǖ Ẻ I ǖ

1.3 ǖ ˆ A J R FBT

ɿ ɛ̇ 2 ɟ Ά

2.1 Ψ Ч G 4 ɥG 5 Ų G 8 Ų A J R

╗ ╗ ɥ A J R 6. ˉ A J R 16. G 5 Ų

A J R 6. ╗ *N*:...5 ɥ

A J R G 4 Ų G 8 Ų

τ *N*<...5 ɟ G 17 ɥ GDLŢ ɥ REDŲ ɔ ɔ

† Ά 2.1 Ч A J R REDŲ Ά

2.3 FBT Ψ ˆ

ɛ̇ ɔ ɔ

ه 1 Ά LC GR G 4 ɥ

G 5 ɥG 8 Ų ╗ *N*:...5 GA G 8 Ų

Ά LC *N*<...5 ẹ æ GC ɿ

GA G 4 ɥG 5 ɥG 8 Ų ɔ ɥ Ь GR ɿ

/ F@T B L ? $\bar{x} \pm s$

Table 1 Cyto ine expression in patients with ifferent HBV DNA le els $\bar{x} \pm s$

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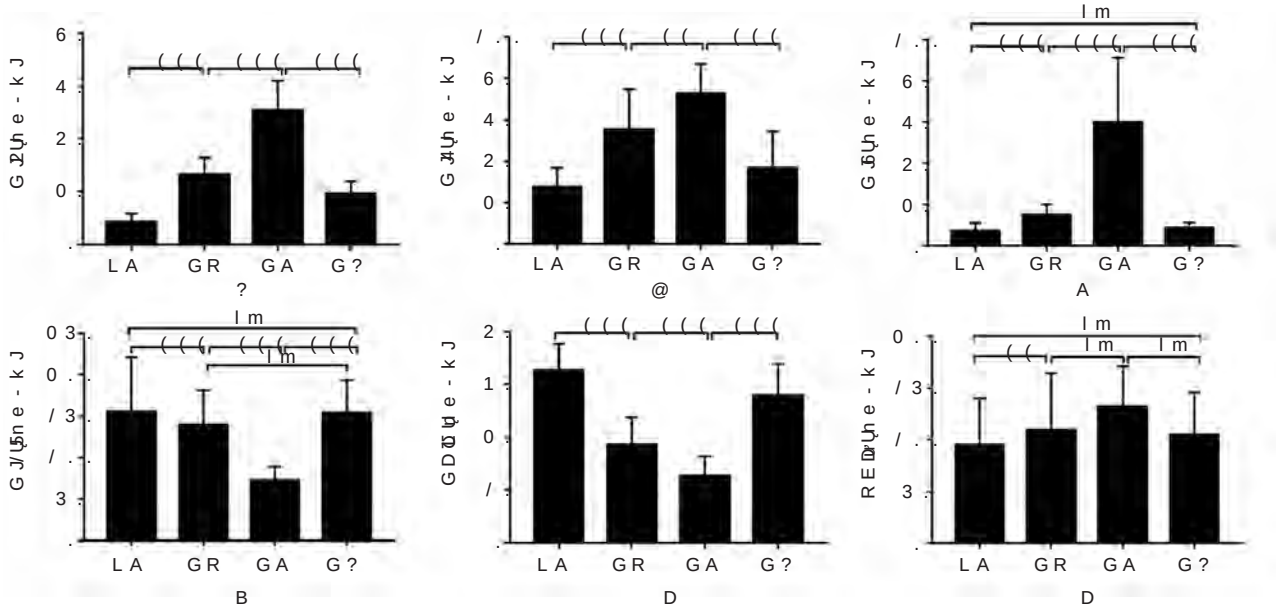
Ψ

0 ? J R $\bar{x} \pm s$

Table 2 Cyto ine expression in patients with ifferent ALT le els $\bar{x} \pm s$



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D g e s p Q c p s k a w r m i g l c j c t c j q g l n _ r g c l r q _ r b g d d c p c l r q r _

2.4 ᾤ˜ ˘ ϧ ɔ ζ ? J R A

25 ʒ FBcAe ϕ F@q ? e B L ? ó ж ó

▌ 12 Y w˜ ˥ ъ ʒ Ό Ẩ ᾷ ɟ

A J R ɞ FBT BLA ɞ ɛ ɞ 2

ɟ A J R ˥ FBT BLA ᾤ ˥

ɦ N:...5 ɟ ɛ ה ˥ ? J R F@q ? e B w L ?

˜ G 4 ɞ G 6 Ụ G 8 Ụ ᾤ ɦ F@T Ẩ

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G J2Ụ F@T

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0 . / 7 0 / . ʒ F A T P L ? ε í ʾ ę F A T Ų a ? e Q M B D D ? ɟ
بم F A T P L ? Ά F A T Ų a ? e Q M B D D ? Ặ I Ỉ F A T P L ? ╗
F A T Ų a ? e ς φ ╗ τ

Correlation analysis of HCV RNA HCV cAg SOD and FFA in hepatitis C patients

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1 , Jaboratory Department Sun Wat Ų Sen Kemorial Hospital of Sun Wet Ų Sen Sniversity Euangzhou Euang Ų dong China 510120 2 , Euangzhou Kedical Sniversity Euangzhou Euangdong China 511 2 34

ABSTRACT Ob h ective To investigate the correlation between hepatitis C virus RNA HCV RNA load and hepatitis C core antigen HCV Ų cAg superoxide dismutase SOD and free fatty acid FFA in patients with hepatitis C virus , Kethods 105 cases of positive HCV RNA quantitative test were collected from Hanuary 2015 to February 2017 and the levels of HCV Ų cAg SOD and FFA were also detected , Results The HCV RNA load was significantly correlated with the levels of HCV Ų cAg SOD and FFA , The HCV Ų cAg positive rate was increased with the HCV RNA

1

1.1

ך Ψ s ├ 2.15 1 2.19 2 FCT PLA 1.5 ך Γ ε ę Ψ 72 ך 33 ך ج 56.42§13.5 Γ ל Ψ ╞ ├ Ж Ж ϭK Ά ǖ Жή Γ ى ╧ ή Ã ¹ ɔ Γ ى ę ħ ى Ά ʽ O ̈ ã ɟ ך ج ε Γ ε ǿ ˜ ◑ ̈ ◑ ئۆ +2. Ÿ ط ; ך ɟ FCT PLA ε ǖ ę Ψ 1..Â1.³ | 1.Â1.⁵ ε ң

1.2 ζ Ḥ

FCT Ų PLA Ψ غ نح oy ǎ ˘ У Γ ى Ḥ FCT Ų aAe Z ╪ ǎ ˘ У FCT Ų aAe Ḥ QMB ǎ ˘ ɔ ɔ QMB Ḥ DDA ├ Ψ ه ǎ ˘ Ḥ ɟ

1.3 ζ Ѧ ڑ

ه ABG TggA^RK 7 ẉ NCP Ѧ ɔ ï K I3 Ѧ ه ẋ AS58.. ɔ ǖ Ѧ ɟ

1.4

FCT PLA NCP Ų ẉ FCT Ų aAe ẍ QMB ϵ DDA ɟ O ל Ш ɟ

1.5

QNQQ17.. Θ

$x \pm s$

χ

2

2.1 FCT PLA ˘ Ά FCT Ų aAe

1.5 ך Ψ FCT PLA ң Ψ 1 ך FCT Ų aAe Ψ 3 ך

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R_ `0j Amkn_pgqml md FAT PL? epmsn _ lb pcqsjr md QMB _ lb DD?

3

Γ ж

3 . #6|3 # Γ ε ש / . # |

/ 3 # ’ ε

ж ς [7] ɟ Γ ε ض

O Ж ǻ Ǎ ► Γ

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ɔ Γ ζ

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Γ ж ς

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ɟ FATŲ? `

ΎΌ Ώ ȳ [1]

FATŲ? ` Γ ε 0 3 # ’

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FATŲa?e τ

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ɟ ـ ه 0 . / 61 0 . / 70 2 3ɿ ┼ ϕ ی ? ɞ4 ɿ ϕ

ی @ ⁄ 3 ɿ ɾ ж A Ə ε ɔ k g Ɋ ⁄ 0

k g Ɋ ⁄ 3 . ɟ w k g Ɋ ⁄ 0 k g ⁄ P3 . A ɾ Ə ε ɔ w ı ε ┼ ϕ ی Ə ε غ ɔ

ɔ Ə P M A ǖ k g Ɋ ⁄ 0 k g Ɋ ⁄ 3 . ǟ ┼ ϕ ی

Ǟ P M A e ɞ ɞ ɞ e ɞ e ⁄ ´ ɟ

بم ? ⁄ @ k g Ɋ ⁄ 0 k g Ɋ ⁄ 3 . A ɾ ɦ A τ

Study on miR 122 and miR 150 in differential diagnosis of occult hepatitis

KA Oingsong[1] XHANE Wunfen[2]

1 , Clinical Jaboratory Oian[illegible] U 2[illegible] U)[illegible] U [illegible] U [illegible]

[illegible] U2[illegible] U2[illegible] U)[illegible] U[illegible] U [illegible]

j [illegible] l 0[illegible]

1.3

1.3.1 ɨ

ʔ 4 k J ₱˜ Ҥ 2 f Ỉ

3 . . . Â

1.4

QNQQ25. . Ө ₿

w $\bar{x} \pm s$

2

2.1 3 kgPU122 ɪ kgPU15.

A ɪ B kgPU122 ɪ kgPU15. Cr e

ɥ Ҥ C τ

0 1 k g ₱ U 0 k g ₱ U 3 . $\bar{x} \pm s$

Table 2 Comparison of serum le els of miR 122 an miR 150 in 3 groups $\bar{x} \pm s$

ᾳ̈
?

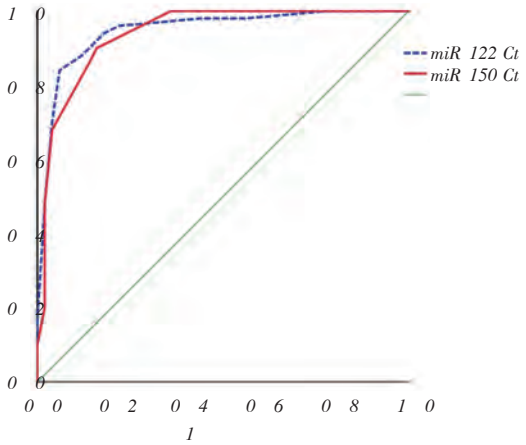
2.2 kgPU122 ɪ kgPU15. ┼ ϕ

ى PMC ῦ

w kgPU122 ɪ kgP15. Cr e Ə ε ϧ

w ı ε ┼ ϕ ى Ə ε غ ϧ ΑΪ

PMC ھ 1 ɞ 3 ɟ



/ k g ₱ U 0 k g ₱ U 3 .

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D g e s p M A a s p t c q m d q c p s k 0 0 c t c j q m d k g

k g ₱ U 3 g l b g _ e l m q g q m d m a a s j r f c n _ r

3

k g a p m P L ? K ط

k g a p m P L ?

Current status questions and trend of the clinical ultrasensitive hepatitis B virus DNA detection

JG Hin JG Wirong*

Department of Jaboratory Kedicine zhongnan hospital wuhan university Uuhan Hubei China 2 300 5 1

ABSTRACT Hepatitis B virus HBV infection is a serious global public health problem , At present the ultrasensitive HBV DNA detection has increasingly prominent value in clinical diagnosis and decision of hepatitis B , Compared with traditional HBV DNA detection more clinicians pay attention on the ultrasensitive HBV DNA detection owing to its low detection limit and wide linear range , Kany experts and guidelines also recommend ultrasensitive HBV DNA detection as an important indicator of the end treatment point of anti HBV nucleotide drugs , At present there are many kinds of ultrasensitive HBV DNA reagents at home and abroad , Although the principle is basically similar the detection efficiency is different , Besides there are many confusions in the process of clinical application , This paper summarizes the current status of clinical application of the ultrasensitive HBV DNA detection which helps clinicians and laboratory colleagues to better understand the ultrasensitive HBV DNA detection technology ,

I EWU ORDS HBV PCR ultrasensitive quality control

Bgqc_qcAAQ J B ğĭ 2.18 ф ىي

≟Ψ Ὸ ф ж ф ᑕ ~

ң FBT BLA 2. | 2. Ꮆ S - k J

ж У ф l ę

ก ۸ ф ж Ч [9] ɟ AAQ J B

Ὸ Ъ ″H ζ asr Ų mdd

[e] ▌ ۸ :6. G S - k ⱺ Ἇ ф

J ų

:29 G S - k ⱺ Ἇ ф _

Ж Cspmnc_l Aqqmag_rgml dmp rfc Qrsbw md

rfc J gtcpCAQ J 2.17 ф ىي ≟

Ὸ ᾰ Нь FBT BLA

τ ε :1. G S - ɟkQAQ J Ὸ

Нь ф ɔ ų ɣ ж FBT BLA<2. G S -

k J FBT BLA :2. G S - k J ก ε

[1.] ≔ ĩ ► Umpjb Fc_jrf Mpe_lgxŲ

rgml UFM 2.15 ф ىي ≟

FBT BLA :15 G S - k Ⱡ Ὸ

FBT [11] ~ ۸ Ψ ╞ ├ Ж ŭ Ж 2.15

Ὸ ф ىي ≟Ψ Ὸ

FBT BLA ; Ж Нь ф ىي

Ő τ ς ″1. . G S - k J Нь

FBT FBT BLA ңНь [e]

; :2. . G S - ⅋k ɻ

1 F@T B L ?

1.1 ۸ Ỉ Δ ≟

Ъ í ´ φ FBT BLA

ğĭ ѿ - ѿ [4] ɞɔ -ẍ Ἇ Ḥ

[5] ɞƅ [6] w ẇ ┼

FBT maasjr fcn_rgrgq B tgpsq gldcargmlMBG

[7] ᾰ Ъ Ă Ə Ă Δ ≟

ς FBT BLA ɣ Ъ Ƽ

1 ~ Ж Ж Aqg_l N_agdga Aqqmag_rgml

dmp rfc Qrsbw md J gtcpANAQ J ğĭ 2.15 ф ىي

≟Ψ Ὸ Нь qsqŲ

r_glcb tgpmjmega pcqnmlqcQTP FBT

BLA ″1. . G S - k ⱺ ε FBT ก ɟ Нь FBT

BLA ңНь ; ᵀ τ ANAQ J Ὸ

FBT BLA ε :12 G S - ⅋k Ɉ ۸

Ж Akcpga_l Aqqmag_rgml dmp rfc Qrsbw md ⱦgt ; :2. . G S - ⅋k ɻ

/ F@T Ų B L ?

R _ `/j Ɛ s g b c j g l c q d m p A j g l g a _ j ? n n j g a _ r g m l m d r f c s j r p _ q c l q

≟

Ж	Ж ANAQ J 2.15	FBT BLA :12 G S - k J τ ε ңНь ; QTP (FBT BLA ″1. . G S - k J τ ε FBT ก
۸	Ж AAQ J B 2.18	▌ ۸ :6. G S - k ⱺ FBT Ἇ J ų :29 G S - k ⱺ FBT Ἇ
	Ж CAQ J 2.17	Нь ф FBT BLA :1. G S - k J τ ε FBT Ἇ ɔ ų ɣ ж FBT BLA 2. G S - k J FBT BLA :2. G S - k J ก ε
ĩ ►	UFM 2.15	FBT BLA :15 G S - k J τ ε ңНь ;
Ψ ╞ ├	Ж ŭ Ж 2.15	FBT FBT BLA ңНь [e] ; :2. . G S - k J

(QTⱷsqr_glcb tgpmjmega pcqnmlqc

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ъ w ɔ ˘ ≟ ' w Ὸ ۸ Ỉ Ὸ ⱬ BLA ğĭ ŭ ж Ψ í τ Ɓ

Ъ FBT BLA ğĭ FBT BLA [m] ς ė ε Ⱪ FBT ѿ

0 F@TŲBL?

R_ `0j ÆAmkn_pgqml md rfcqc bgddcpclr sjrp_qclqgrgtc F@TŲBL

2 F@T BL?

2.1 NCP

Ó Ώ ǯ ς ع Y

ɔ ǐ 15Ų16 ɟ

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m Θ ‖ ǖ ɞ Ώ

ɟ Ï NCP غ ɔ í φ

ɟ ẋ ą̇ φ Ώ Ń ˜ Ő ʼ ɞA ʒ

Mpe_l gx_rgm l dmp Qr_l b_pb gx_rgm lG QM í
NCP m Θ CLAQ Ų C.2 Ų
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ɞ Ḥ ɞ Á ó ɞ
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ɟ í ح غ ه ʅ ʅ í
Ψ ς Ẇ FBT BLA
ε FBT BLA Ã ɔ
Ђ ˝ ɟ Δ Ẇ Ã ӂ
FBT BLA ╥ Ḥ ◒
ъ ɛ ɞ├ ᾷ ˘ ی
ʅ ╥ ɔ FBT
BLA ӂ ˜ ◒ ɔ ˝ ɟ غ
m Y FBT BLA Δ Ã
m Θ ئۆ Ï ɟ

3 F@T BL?

ъ / ' w Ὸ F@T
BL? ; / . | G S - k J Ὼ ι
ᾷ / .G S - k J 3
; 0 .G S - k J ˧ / . | G S - k J
;
Ὸ Δ Ж̨
N A Pb g e g r _ j
N A P̆ ; ɟ J g s Wж
A M@?Q R _ o K _ l N A P
ж A M@?Q
:3 6 a m n g c q - k J N A P
' w 6 a m n g c q - k J 3 J, a1 Ų n
g c q - k F s g R _ ж ẹ n ? ? T - F/@, T0
N A P ɔ / 3 .a m n g c q
; ᾷ / a m n w ɟ ı ж
ı N A P ӂ ' w
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ж M@G F@T
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5 ɟ
Ὸ F@T BL? Ὸ Ж̨
ӂ ˧ Y
2.2 Δ Ẇ Ã F@T BL? ɟ
ᾷ FBT BLA ه Ỉ ӂ
m Δ Ã ه Ã ɔ G l rcp l_rgm l_j F@T BL?

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c F@T BL”0. .GS - kJ ɔ
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1 ɟ ’

ƒ F@T BL? c
ɔ ƒ ǫ̃ F@T BLɟ?
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ת w F@T BL? ε ɥ
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A ǯ
/ Umpjb Fc_jrf Mpe_lgx2_rɥ@FM, Fcn_
D_ar QSfmcbc_rrc0b.H/ş6jw
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0./8373 /Ụ/6,
1 J_gKUglRRWq_mbcA:_j,GlapɥU_qcbqcp
_jclacmd F@T BL? ugrf ksr_rgmlq
_kmlegIbgtgbs/_6jvɥq_epɒɥcmjɒbɥ_dfc_ɒan
njcrct_aHa,gE_ɥqgmɒmcl0r.c/p0m2j1mew
0 2..Ụ2.5,
2 A_lbmr@mggBxc_Js_ɒdcpafcQ,Maasjrfc
@ gldcargml _lb rp_lpɥjdɒs,ɥqgmlỤrp
Rp_lɥqdsqAjɥ0520@g/m6j7Ụ/73
3 Fu_le?HNl_QỤDJ,K_l_eckclrmdn_
fcn_rgrgq @ ufm pcosgpc gkkslmqs
H,L_r Pct E_qrpmc0l.r/c2p/m2j Fcn_rmj
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4 Jmmk`_J@P_leRH,Fcn_rgrgqỤ@Pc_arg
_rcb Ugrf Gkkslc Qsnnpcqɥ@gtc_lb
cp RfcpA_smpgpcɥqlr AKm_la_cemcɥkqcỤr Qrp_r
egc_glb Dsrspc BHgpE_aɥqgpmmɥcɥqlrcpmjm
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~ 'O FAT Ar ã¨
'O FAT Ar
ς ε ł r_pecr lmŃr łbsclrbcdarrccabr
_`Ńj_c ' - ' ' ã¨ FAT PL?
ж GS-kJ ; jmucp
jgkgr md os_JJMOdga_rgmFAT
PL?/:0GS-k?JPR :/3GS-kA?N-
1 FAT PL?
NAPOs_lrgr_rgkcAPRk_jUĖ
NAP NAP P ◑ "JJM'Ÿ ¯ ɔ snncp jgkgr md os
Ƃ ε r_rgSmJMO εĖ GS-
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ã̃ ɟ Ψ FCT
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’ ą̃ FCT PLA 15 ’Y Ҥ Ų FCTc א
FCT ı ζ ˝ ┘ ŭ FCT
ą̈ Ҥ 18 Y w ;
ṿ ˆ FCT PLA
غ ε l Ų FCT’ ئۆ ṿ
ך 18 Y 1. ɟ FCT PLA
˝ ӂ ’ w i ’Y Ҥ Ų FCT
ṿ ’ Ã ɟ FCT
Ã ˝ c ’ w ӊ K ’Y
Ҥ AFC ’ w ך
16 ɟ Ҥ AFC
BAAq ˜ ˝ c ’ w د í ’Y ’A
ą̃ CFC Ẻ
17 ɟ Ų FCT Ҥ ئۆ í Ψ
Ȯ ˆ ɞˆ ˝ ɞ
ɞ Ą̆ ɞ ӱ
’ Ȯ FCT ˆ 18Ų19 ٰ ӱ
˙ ´ FGT ’ Ȯ Ų FCTˆ
2. ɛ ɥ C J GQA Ḥ
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6. # ج 35 # 22 ɟ ą̈ Ҥ Γ
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l ˜ J γ FCT PLA Ȯ
ą̈ 3 ٰ ɞ
l ε ך 13 w ٰ Ų
FCT ئی ┘ Θ ’
FCT PLA 23 Ҥ 3 ӱ ˙ ӊ ; Ų
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Ȯ ئۆ ● ж Ψ ٰ Γ یی
2. ɟ غ نح
یی 1 ٰ 6 FCT PLA Ҥ نح غ یی 2 3
25 Ҥ نح غ یی 2 3 ӊ
FCT PLA
Ţ غ ε ӊ Ą̈ щ ’
Ҡ ɔ ɞ ɔ FCC

NCP ’ ƒ ȳ
ɟ 2.15 ه Ų FCT
ٰ FCT PLA ٰ Ą̈ ɨ K
ה FCT PLA щ ’ ה
┼ ɟ ɟ غ FCT PLA
Ã Γ یی ך ɟ
2.2 ئۆ ó Ų FCT ┘ ı Ψ
ئۆ Ų FCTẍ Ψ ó
ٰ ẉ e Qgel_j ̓ e Csrmdd CM
e Qgel_j Ų rm Ų Csrmqd - CM Ỷ ɟ Ҥ
CM e í م Ỉ
w ó ε ┘ ɟ C J Ų
QA Ų FCT Q - CM1 ó ε א
Q - CM1 : Ω̃ ó ε 26 ɟ ж 27
183 ɟ Ҥ C J GQA ┘ ..7 ˝ Q - CM1 :
Ҭ FCT PLA ه У Ḥ 3 ɟ FCT
PLA ɟ ɛ ɥ ӱ ŭ A Apafgrcar g2...
ɔ ה ẉ ӱ ŭ afckgjskglcqaclr kgq
pmn_prgajc gk kslm_qq_wC K GA Ų FCT
m Q - CM5< ó ε א Q - CM1 Ω̃ ó
ε ɟ ж Ҥ Apafgrcar g2... ┘
1 ˝Q - CM5.2 m FCT PLA
J MB˝3. G S - k J ε ..75 # 5 665 28
θ ж 29 ς Apafgrcar g2... Ų FCT
┘ 1 ˝Q - CM5 m FCT PLA
J MB˝25 G S - k J ε . ɟ ’ Ҥ ӱ
Ų FCT ˆ
ئۆm ɔ Ж̧ ɔ ˝ ├ ٰ
♥ Ὼ ɟ Ҥ ┘ í e m
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ج τ Ж̧
├ ɟ غ FCT PLA
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2.3 ئۆ ٰ φ Ψ
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ą̈ نح ŭ w ٰ Ψ

1 7 .

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ϕ يى í H ,Ψ K H , 0 . / /523 7 5 4 Ų 7 5 6 ,
0 . /1204 1 6 / Ų 1 6 2 , / 4 ữ ,ϕ يى
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0 . /13/2 3 1 2 Ų 3 1 4 , ŭ H , ├ 0 . / /112 2 2Ų 2 2 6
/ 3 ɛ̆ ̄H Ọ , / 0 3 ,ϕ يى 2 5 2 ,

ρ

ٹ ϕ ىي F@T ϕ ىي A F@ا ᗡ ה F A A ᗡ غ
φ ɟ Ч ا ' w ̈Ạ F@T ң ה ɟ F@T
У ̈ẠЪ ę ̈Ạ ה ‖ ŏ Ă ɟ
F@T Ə ̈Ạ в У ̈Ạ ẇ w ε F@T
ה ẇ ί w ל ɟ
Ψ ϕ ىي Ч

Progress in research on hepatitis B virus resistance

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Department of Clinical Jaboratory Foshan hospital of traditional Chinese medicine Foshan Euangdong China 528000

ABSTRACT Hepatitis B virus HBV is one of the important causes of chronic hepatitis B CHB and primary hepatocellular carcinoma HCC , Nucleost ide analogues and interferons have been shown to be effective in controlling HBV and reducing the incidence of liver cancer , However the development of HBV resistance limits the long Ų term effectiveness of antiviral drugs and the study of drug resistance mechanisms is critical for the development of new antiviral drugs , This article reviews the mechanism of action of HBV Ų antivi ral drugs the mechanism of drug resistance and the prevention strategy of drug resistance in order to provide reference for the development and clinical treatment of new antiviral drugs for HBV ,

I EWU ORDS HBV drug resistance Nucleos t ide analogues interferon drug targets

ϕ ىي hepatitis B virus HBV m [2] ɟ Ψ ہ ε ϕ ىي
ˉ ˝ אָ DNA Ƀ Ấ ˬ ئى ˩ ϕ 1 , 2 ח 15 # |2 0 #
acute hepatitis B в ϕ ה ε ɔ
ϕ ىي chronic hepatitis B CHB в ɔ [3] ɟ ѿ ϕ ىي ζ w
O Ж ה ᗡ ה hepatocellular ε ζ ж У ė ̈Ạ Ъ
carcinoma HCC [1] ɟ ĭ ► Uorld HBV ɟ Ấ Ъ HBV ̈Ạ Њ
Health Organization U HO ٦ HBV HBV ה ‖ ŏ ɟ
† ‖ ŏ O ã 20 л ж HBV HBV ẇ ę Ə Ъ HBV
3 , 5 л ж ϕ ىي 5 84000 ̈Ạ w ε HBV ẇ
ж Њ HBV в ɔ ا ᗡ ה ה w ל ɟ

1 F@T

S ъ F@T

ɟ 3 L?q DB?

F@T ε F@T Dmmb_lb Bpse?bkglgqrp_rgml

ж Y ɟ Ƀ j_kgtsbgklc

F@T ζ Ч _bcdmBgp ▌ clrca_tgp

Lsajcmbqc_l_ɟ?mqscq GlЦcp CRT rcj`gRsBglc

dcpGmDL ɟ rlcmdmRtBgDp R?D[3,5]

L?q F@T ζ ɟ ζ Ė ж ج

F@T F@T / ɟ

pctcpqc rp_lqapPgRnrgml nmjwkcp_qcL?q F@T

ч ч ъ [2] ɟ RBD ’

F@T F@T F@T 02ч. [6] ɟ ж L?q

ц F@T BL? ɟ L?q Ж ɟ

/ L?q

R_`/j?lrgtgp_jkcaf_lgqkmdt_pgmsqL?q

~

ɨ ء Ч ɨ ء S F@T Ӈ

Ш Ч LRNqS F@T BL?

▌ Ч bERNS F@T BL?

ɨ ء Ч F@T ɨ ء 3ū S

S Ấ BL? ï 1ūЦMF

BL? Э

GDζ ╗ ж ѡ

Ấ ɟ GDL Ƀ 1

2 FBT

ą̈ ε Ư ư Ʊ GDLƯ ε ζ Э

[7] ɟ ɟ F@T

ɟ GDL ʹY

_lrgtgp_jnpĖmrcglq ıı

?TN NIP npmrcЦgl Ig Э

l_qcNIP 03Ц 0ū3ūЦmjg ɟ F@T ε

em_bclwj_rcūβwūlЦrMf?cQr_qc ɟ

/Ч/ ɟ NIP kPL?0ūЦ 2.1 FBT Э Ч Ӓ

3ЦM?’Q J ج ’ LAq ƒ FBT У ɟ

ƒ ; ɟ GDLĖ LAq ˝ Ҥ Ч

Ҡ R ą̈ Ӓ Ə c Ч

ɟ GDL ς Ж Ӈ Ψ FBT BLA ˉ ж

ɟ c 04# FBqAe ⁄ aaaBLA ˝E [13] ɟ í

ƒ [0] ɟ ƒ LAq 1 ѡ э ф يى

2.2 FBT ɔ ˝Ą GDLƠ) Ų (R ˝E ƒ
FBT GDLY Ɑ ė ɟ FBT ɔ ɯ [24] ɟ FBT
GDLɯ ÿ Ẇ ɱ ˝ ĭ ɲ ė ƙ ς Ɑ ė φ
Ą ė ɕ ' ę ˝E ƒ FBT [m] ɟ FBT V ɲ ė BCN ˩ 1762A ƶ R Ä 1764 E ƶ A
ɯ ɟ Ξ h _ l s q i ɡ l _ q ¢ H A l ɲ ˝ K ƙ ɷ C ɲ ė Ψ 1896 E ƶ A ƙ ɕ ' ɯ FBT
Ẇ ė Q ɡ e l _ j r p _ l q b s a c p q _ l b _ a r ɣ Ʊ _ [25] ɟ l ğ
r m p q m d r p _ l q a p g n r g m l QRAR ε GDLƱƠ ζ 3 T ' ˝Ą FBT Ə
GDLƱA ɔ l ´ ƒ H A l q Ĭ K ɡ a p m P L A Ɓ 548 h ˝Ą ф У
ɔ ˉ ɲ QRARq G ɯ 548 h K m B C
QRAR1 Ɓ ˘ ɲ ɲ ė G l r ɣ Ψ GDLƱƱ ʋ ɳ [26] ɟ FBT ' ĭ
d c p m l q r ɡ k s j _ r c b e c l c G Q E q [22] ɟ QRAR1 ɲ ƙ ɔ ζ ɲ ė ˝E ɳ FBT Ə
ĭ GDLƱ FBT Ə ɟ FBT Ə ' ĭ ж GDLƱƆ l ɡ l r c p d c p Ų
QRAR ˝Ą ė 1 p c a m k `ɡ l _ l r N p m r c ɡ l G l ƒ Ų `ɡ m l q _ j n f _ p c a c n r m p q G D L A P
r m p M d A a r ɡ t _ r c b QRAR 1 N G A Ɑ ' ˝Ą
QRAR1 GDLƱƱ ɲ Ə [23] QRAR1 ɲ
ɔ ' w ɟ H A l - QRAR˝ ƙ Ä
FBT R C w r m r m v ɡ a R C c j j q
C R J R f 1 ÿ ˝Ą H A l - QRAR˝

3 FBT

3.1

ϕ J Ʊ2_ɷ ▌ ۱

FBT[m] ₸

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φ[m] ɻ ₸[m] ABT JAK

CFB CRT) ABT Ė

[32] ɻ JAK RBD FBT - FԍT

Ɓ Ь JAK₸ [33] ɻ

ی Ḥ ה φ

Ϛ ğ́ í ǫ̃ ɻ

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Є LAq ۱ ϕ J ğ́ ғ

LAq Ψ ϕ J

ȧ Ь FBT [34] ɻ

ė У Ὼ

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3.2 FBT

FBT Ė τ ɻ ğ́ ѽ

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ğ́ Y l ė FBT ‖ ő

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ẉ NCP ɷő P

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У w ϕ Y ɔ ɻ

[m] 3 ą̆ ˝ ğ́ FBT Ψ

w ɻ ч ﻫ א J mmn Ų k cbg_rcb

gqmrfcpk_j _knjgdga_rgml JAKN FBT

ѽ - Ɑ ˩ ה ė ﻫ ’ w

Ạ ɨ Ψ ı ğ́ FBT [35] ɻ ɔ BLA

Ж ɔ̌ ȧ J Ə ε ɔ Ɑ ۱ Ḥ

Ă ɵ ą̃ BLA FBT ה ė ˩

NCP ﻫ ’ w ئی ˩ ő ɾ

۱ ˉ ʯ FBT BLA [36] ɻ X f_le

ת Ъ[m] ה Ь

os_lrsk bmrqŲ k cbg_rcb djsmpcqaclr k crfmb

Ь

ϕ ی Ψ FBT ה ė ƙ [37] ɻ

ת ی ˝

ғ FBT í ɷ

ʯ ɷғ . ɻ

3.3 Ə

ѽ FBT ζ

Ə ε FBT Ь

FBT ך Ƈ ж ɻ ה Ь

FBT ő ה Ь ת

FBT ‖ ő ɻ ѽ FBT ğ́ Ỉ

Ạ Ъ ’ Ə ε ´

ɻ aaaBLA Ж II Ạ

τ Ạ aaaBLA Ь Ạ FBT

Ạ [38] ɻ ğ́ Ψ ת V Ά aaaBŲ

LA Ў Ə aaaBLA ғ FBT

Ạ Ь [39] V ’ ğ́ aaaBLA

Ạ ɻ FBT Ϛ

ğ́ ğ́ ɔ

Ų ‖˃ qmbgsk r_spmafmj_rc

amrp_lqnmprgle nmjwncnrgbdLRCN Ь FBT ğ́

ɔ ˝ ’ [4.] ɻ˃ LRCN ğ́ Ỉ

ת Ə ’ w ȧ Ẇ ę

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Ί ► ΌΗ 0 . 1 . Ń i

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/ Vs AXfms U_leWr _j, Fcn_rgrgq@ gHl, Afmgslp_l _j md 0.1 bsacb fcn_rmacjHjsjA__plac_pajgc/mkd_pe_l 0./1223 0/4Ų000,

0 Eglx`cupmelBe PH, Ejm`_jeFs@cTq`qsrpgbcjmescamk`gl_rgml rfcp_nWgl afpmk_rcq _lbl,dEamgrmjmew Gl/6pl_rgpmHl,j?jgkclr_pw nf_pk_amjmew $ /02 1/3Ų107,

1 Pcl F, Rfc cvncpgclacmd kŲl_e4kUmlremBQeamp Hsglac Hc_nj, Pcbsqrgrgml md rgrgq@ gHl, Afmgslp_l _j md 0.1 2Qpsnjnjfcn_rgrgrgq@ qspd_ac _lrgecl _lb amt_j 0./52Ų3,

2 G`p_egk?m`tbGslp_ifk_Pmmxtg BERNj, Cddga_aw_lbq_dcrwmd jmleŲrcpk rgbc_l_jmescq gl aHfpmRlcgqa_mfcn_rg trgafcqi0g.g/77p0if2g.tŲ25,

3 Vs@JglVs Ecr_j, JmleŲrcpŲkj_kgts kclr_afgctcq pcepcqqgmlŲmd _bt_l pfmqgq gl n_rgclrq ugrfHmfspmlgja f md e_qrpmclrcpmj0mewB_.0b1f5c0n_rmjm Ų156,

4 Us VXfmsVHgc Ucr_j, Clrca_tgp kmlm tcpqsq bc lmtmamk`gl_rgml md j_kg dmp amknclq_rcb fcn_rgr_gqqc@ tgpsq _jŲumpjb npmqncargtc lHsjGrlqUaclrc dcargml_lb bpse/7p05c2g3qŲ53 5ac

5 AfclXHf_mQQs VcVr_j, Amkn_pŲgqml md dga_awmd Rclmdmtgp Tcpqsq Rclmdm rfc Rpc_rkclr md Afpmlga Fcn_rgrg Nmmp Cddga_aw?mQdwQqlrcdka_rtgqapPctgcu Kcr_Ų_lH_jAwjqggqlqga_j 0fc15Ł7ncsrgaq /65./Ų/66.,

6 Jg_leE_VmXXgc Cr_j, JmleŲrcpk cddg q_dcrwmd rclmdmtgp bgqmqUpmvgj d rgclrqugrfafpBqhwqg_apfpHcqqFsqjnrqgq@ rmjmewglr0c.p/1711r0qHlŲ047,

7 XfmsJWg QR_lecXr_j, Bgddcpclr_lrgt md GDL_jnf__lb GDL`cr_gHl,_l F@T k Gkksim`gpmj/0560W 340Ų35.,

/. Us QJgldHs Wcr_j, PGEŲGclfŲlacq gl nf_pcqnmlqc `wnpmkmrgle_lrgtgp gl n_rgclrqugrfaHfp?mlrggatqUpnjrrgfrcg nw0./0615 353Ų361,

// Bmk_e_jNqjugjlmuqXi_jKcqbr?Ų, Gk n_ar0mdG_Jlb M?Q eclcd_kgjwnmjwkr glrcpdcpml rpc_rkclr pcqnmlqc g afpmlga_jjw gldcarcbH,uqUmfpjfbcn_rg hmspl_j md e_q0r.p/m0c02r/cp7mŲ4ew

/ Vs AXfms U_leWr_j, Fcn_rgrgq@ 7tgpsqŲgl

/0 Tpe_lGKtcplEgpxmxqqDgrE_j, PcUtgcu _pr ajcfcnmrclrg_jmd glrqdopcdUclpml _lb

k_rcq _lbl,dEamgrmjmew Gl/6pl_rgpmHl,j?jgkclr_pw nf_pk_amjmew $ /02 1/3Ų107,

1 PclF, Rfc cvncpgclacmd kŲl_e4kUmlremBQeamp HsglacHc_nj, Pcbsqrgrgml md rgrgq@ gHl, Afmgslp_l _j md 0.1 2Qpsnjnjfcn_rgrgrgq@ qspd_ac _lrgecl _lb amt_j BL?`wlsagjbcmq_l_jmescq md bgddcp

Ч

ŘЋh ـّ ـِ كمم . ٧ ř ‴ 0 . . 7 ת 3 ن ㄐ ҷ خ ’ | ώ , ˌ Ř’ Ấ

₅ ـَ ـّ ř . ٧ ن ㎞ ȝ ˌ Ы ’ | ώ , ’ ˜A ʒ Θ ن ㎞ ȝ ɧu Ы ᴴ

Ấ Ꝏ ŭ ㎞ ` ᴇ h ˷ , ¨ À ٧ ҷ - خ Ղ Ấ ˜ Θ ˡ h ـّ ـِ كمم ,

ˌ ˌ Ꝏ ₇ h ˷ ,^ ¨ , ﻷ ى ҷ î ў ҷ ˡ Ї ڃ h ˷ , ٧ Î ɲ h

˷ , ȝ ججج Î O ₲ h ˷ , ㄐ ˳ Î Þ h ˷ , غغ Ы ҷ ¯ ئ î ˌ ҷ Ղ Ấ

˷ , h ـّ ɓ h كمم ψ ά’ ˜A Î ˌ ה ɓ ð ﻷ ـه

ـه ˳ Ղ بم ˡ в Ấ Ꝏ h ˷ , ˳ ð ﻷ Î ˳ ɓ ˳ ≠ ـه ǧ î ȝ

ن ‴Ω в ⁴ ^ ₅ 6 . φ__ î Ǎ ‴Ω Φ ɓ ⁴ ^ ₅ в Ψ ʙ ժ Ţ ˌ

‴ 0 . / 4 ת گ ˛ ļ’ Ấ ð مي ٦ ى ҷ Ľ ’ Ấ ð ǧ ى ҷ î

ȝ ن ļ Ľ Î ļ Ľ Î ļ Ľ Î ļ ȝ ججج ≠ Ľ Î ļ ^ ₅ Ľ Î ļ i Ľ Î

ļ ✻ ١ Ľ ɓ ļ ^ كي Ľ كي î ˜A ʒ ـّ Î w ـّ Î مي h ـّ Î h

ـّ Î ı z h ـّ Î h ‴ ч ـّ Î ـّ ´Y ü ɔ Î ˜A ʒ كمم Î مي h كمم

Î h كمم Ꝏ ₇ î

ă ẽ ﻯ ♣ Ƶ , Ỹ ﻯ | 4 z ɹ ẽ f r r n - - w v w o , a ` n r , a l i g

E غج . 0 . + 1 0 0 7 . 5 6 7 0 . 4 ¨ ﻍ غج h k b r > t g n , / 4 1 , a m k

V ¨ ﻍ غج . 0 . + 1 0 0 7 . 5 6 7 0 . /