

5HVHDFK \$UWLFOH

20,&6 ,QWH

(IILFDF\ DQG 6DIHW\ RI D 7RSLFDQ WHIGLDWULF \$ 5DQGRPLJHG 3KDVH , , , &RQWUROOHG 7ULDO

3DWULFH 30DQWLQ HDG %HQ %HFKHU
'HUPDWRORJLVW DQG 3HGLDWULFLDQ +HDG RI 'HUPDWRORJIA 8QLW &HQWHU +RVSLWDOLHU GH &RUQRXD
+HDG RI &OLQLFDO 'HYHORSPHQW 6NLQ 5HVHDFK &HQWHU +{WHO 'LHX 6DLQW -DFTXH 3LHUUH }DEUH
3HGLDWULFLDQ +HDG RI 3HGLDWULFLDQ 8QLW %DVKLU +DPJD &KLOGUHQ V +RVSLWDO %DE 6DDGRXQ &K
&RUUHVSRQGLQJ LIXWKRHU 5LEHW &HQWHU IRU 6NLQ 5HVHDFK +{WHO 'LHX 6DLQW -DFTXH 3LHUUH }
(PDLOUJLQLH ULEHW#SLHUUH IDEUH FRP

5HFHLYHG 20DQWLQ \$FFHSWHG 30DQWLQ 3XEOLVKHG 30DQWLQ
&RSULJKW 30DQWLQ 3 HW DO 7KLV LV DQ RSHQ DFFHVV DUWLFOH GLVWULEXWHG XQGDU WKH WHUPV
XVH GLVWULEXWLRQ DQG UHSURGXFWRQ LQ DQ\ PHGLXP SURYLGHG WKH RULJLQDO DXWKRU DQG VRXU

\$EVWUDFW

2EMHFVLYDGOH FDS LV D PXOWLIDFWRULDO SHGLDWULF VNLQ FRQGLWLRQ FKDU
VFDOS IODNLQJ 7KH DLP RI WKLV LQWHUQDWLRQDO SKDVH , , , RSHQ ODEHOHG
GHPRQVWUDWH WKH HIILFDF\ DQG VDIHW\ RI D SHGLDWULF JHO VSULQJ ZDWHU J
JO\FHULGHV JLQF VXOIDWH LQ DGGLWLRQ WR VWDQGDUGLJHG K\JLHQ LQ LQI
PRGHUDWH VHERUUKHLF GHUPDWLWL

0HWKRGLQJ WKH ZHHN VWXG\ SHULRG LQIDQV ZHUH UDQGRPO\ DVVLJQH V
Q DSSOLHG EIRUH D VWDQGDUGLJHG VKDPSRR HYHU\ GD\ IURP WKH LQFOXV
VHFRQG RU WKLV GD\ IURP 'D\ WR 'D\ RU RQO\ WKH GDLO\ VKDPSRR FRQWUR
SXEOLVKHG UHIHUHQFH VFRUH D WRWDO OHVLRQ VFRUH FRPELQLQJ PHDVXUHV R
HDFK VFDOS TXDGUDQW UDQJH ZDV XVHG WR HYDOXDWH HIILFDF\

5HVXOWV LILFDQWO\ JUHDWHU LPSURYHPHQWV LQ WKH WRWDO OHVLRQ VFRUH V
FRPSDUHG ZLWK WKRVH LQ WKH FRQWURO JURXS DW ' " YHUVXV " YHUVXV
" S DQG " YHUVXV " S &RPSOHWH UHFHYHU\ Z
LQIDQV LQ WKH JHO JURXS FRPSDUHG ZLWK RQO\ LQ WKH FRQWURO JURXS S
REVHUYHG LQ PRUH WKDQ RI LQIDQV

&RQFOXVLYDGOH FDS JHO HIILFLHQWO\ UHGXFHG 3LW\ULDVLV FDSLWLV IURP
DQG WROHUDQFH ZDV VDWLVIDFWRU\ LQ WKLV VSHFLILF SRSXODWLRQ 7KLV JHO
JRRG DOWHUQDWLYH WR FRPPRQO\ XVHG WUHDWPHQWV &RPELQHG ZLWK XVH RI D
WRSLFDQ FDUH RI LQIDQV ZLWK FUDGOH FDS ZLWK RU ZLWKRXW PLOG WR PRGHU

.HIZRUGUDGOH FDS ,QIDQV 0LOG SURGXFWLQJ VHERUUKHLF NEQV WKDW HQ
GHUPDWLWL 3HGLDWULF JHO 7RSLFDQ WHIGLDWULF QWURGXFWLRQ DOGRLYHG FRQWUROOHG
WULDO 6FDOS GHUPDWRVHV \HDVV > @

,QWURGXFWLRQ

'U\ VFDOS DQG VHERUUKHLF GHUPDWLWL DUH KURORJIA SURGXFWV
VFDOS PDQLHVWDWLRQV RGLVWULFDO WHIGLDWULF WHIGLDWULF WHIGLDWULF
6HERUUKHLF GHUPDWLWL VFRUH SURGXFWV WHIGLDWULF WHIGLDWULF
GHUPDWLWL VFRUH SURGXFWV RI DQ\ DJH ZLWK DJH DQ\ LQGHQFH RI WR
LQ DGXOWV > @ &UDGOH FDS RU 3LW\ULDVLV VFRUH SURGXFWV WHIGLDWULF
RFFXUV LQ QHZRUQV PRVW IUHTXHQWV DUH SURGXFWV WHIGLDWULF WHIGLDWULF
> @H FRPPRQ HWRORJIA LV D FRQYHODWLYH WHIGLDWULF WHIGLDWULF
LQFUHDVHG VHEDFRXV JODQG VHFUWLYH WHIGLDWULF WHIGLDWULF WHIGLDWULF
PLFURGLVWULF WHIGLDWULF WHIGLDWULF WHIGLDWULF WHIGLDWULF WHIGLDWULF
LQGLYLGXDO VHQLWLWLW\ LQFOXGLQJ WHIGLDWULF WHIGLDWULF WHIGLDWULF
FRUQRHFWHV DQG WKHLU SUHSDURJWHG WHIGLDWULF WHIGLDWULF WHIGLDWULF
GULYHQ GLVRHGHUWK RJO\ DQ\ LQ 6'
LV UHODWHG WR WKLV WHIGLDWULF WHIGLDWULF WHIGLDWULF WHIGLDWULF
WKUHH PHFKDQLPV L SURGXFWLRQ RI OLSDVHV DQG SKRVSKROLSDVHV WKDW
LPSDLU HSLGHUPDO EDUULHU IXQFWLRQ LL DQ LQFUHDVHG LQ WKH ORFDO

LQ WKH FRQWURO JURXS ~~RELQGNFOHJ~~ ~~QNDLQJJKWDIPS~~ RRQ WKH FRQWURO ~~WJURKDS~~ V
 H WDUJHW QXPEHU RI VXEMHFWV ~~WRXEHWLRQ~~ ~~FDXGHGRQ~~ ~~HDFKQURR~~ ~~SDZDQ~~ ~~HXQ~~ Q
 L H D WRWDO RI VXEMHFWV :H ~~WRVHD~~ ~~WRHGL~~ ~~QEVK~~ ~~GDHQ~~ ~~WDS~~ ~~GRWLRQ~~ ~~DDQGX~~ ~~EMHFW~~
 LQ HDFK JURXS L H VXEMHFWV GHYLDWLRQV GD\ GHOD\ WR ODVW YLVLV
 IRU WUDFKHLWLW DQG EURQFKLRQLWLV

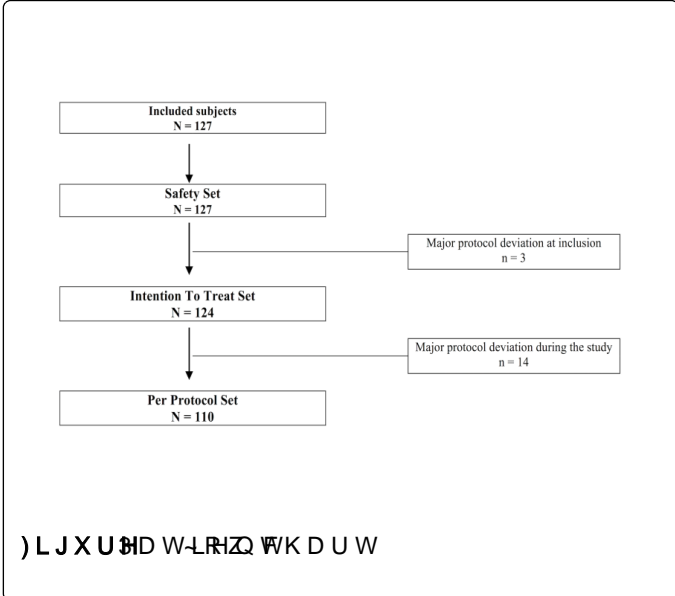
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 UHTXHVWHG LQ WKH SURWRFRQ LQ DOO EX
 ,QIDQWV ZHUH UDQGRPL]HG DFFRUGLQJ ~~WR~~ ~~EMHFWV~~ ~~QRO~~ ~~PHGLD~~ ~~QV~~ ~~UHDV~~ ~~RQV~~ ~~IF~~
 UDQGRPL]DWLRQ ZLWK D UDWLR DQG ~~VXEMHFW~~ ~~UR~~ ~~W~~ ~~DP~~ ~~LUXV~~ ~~GLD~~ ~~BUKH~~ ~~FO~~ ~~XY~~ ~~HS~~
 WR HLWKHU WKH JHO JURXS RU WKH FRQWURO JURXS

6WDWLWVWLFDO DQDO\VLV 3DWLHQW FGDUDFWHULVWLFV DW EDVH
 \$W EDVHOLQH ' LQIDQWV FGDUDFWHULVWLFV ~~WR~~ ~~EMHFWV~~ ~~ZHUH~~ ~~FRPSOH~~ ~~HG~~ ~~XYHU~~ ~~W~~ ~~EHU~~
 &KL VTXDUH WHVW RU)LVKHUdV H[DFW ~~JURXS~~ ~~IRU~~ ~~TXDQ~~ ~~W~~ ~~LYH~~ ~~UL~~ ~~W~~ ~~LD~~ ~~DQ~~
 6WXGHQW V 7 WHVW IRU LQGHSHQGHQW VDP SOHV RI TXDQWLWDLWH YDULDEOHV
 7/6 ZDV DVVHVHG XVLQJ WKH 6WXGHQW ~~W~~ ~~K~~ ~~V~~ ~~U~~ ~~D~~ ~~F~~ ~~W~~ ~~H~~ ~~U~~ ~~L~~ ~~W~~ ~~D~~ ~~Q~~ ~~X~~ ~~S~~ ~~L~~ ~~O~~ ~~R~~ ~~R~~ ~~W~~ ~~H~~ ~~V~~ ~~U~~ ~~X~~ ~~H~~ ~~W~~
 QRQ QRUPDO GLVWULEXWLRQ %HWZHHQ JURXS FRPSDULVRQ RI WKH FKDQJH
 IURP EDVHOLQH IRU HUIWKHPD DQG GLVFRPIRUW VLJQV ZDV SHUIRUPHG XVLQJ
 WKH &RFKUDQ ODQWHO +DHQV]HUIWKHPD :LWKLQ JURXS WLPH
 DVVHVHG XVLQJ WKH :LOFR[RQdV WHVW ~~WR~~ ~~U~~ ~~SD~~ ~~LUHG~~ ~~VDP~~ ~~SOHV~~ ~~IRU~~ ~~WKH~~ ~~7/6~~ ~~DQG~~
 WKH 0F1HPDUdV WHVW IRU HUIWKHPD DQG GLVFRPIRUW VLJQV
 HUURU ZDV ~~W~~ ~~R~~ ~~O~~ ~~W~~ ~~G~~ ~~H~~ ~~G~~ ~~D~~ ~~Q~~ ~~G~~

5HVXOWV

3DUWLFLSDQWV

)URP)HEUXDU\ WR 2FWREHU LQIDQWV ZHUH UDQGRPL]HG LQWR
 WKH SHGLDWULF JHO JURXS DQG UHW WKH FRQWURO JURXS)LJXUH
 VXEMHFWV IURP WKH JHO JURXS KDG 0DQ PDMRU SURWRFRQ GHYLDWLRQ DW
 LQFOXVLRQ LQIDQWV KDG VZHHW DOPRQGLQ RU ROLYH RLO DSSOLHG WR W
 VFDOS ZLWKLQ WKH GD\ SUHFHGLQJ LQFOXVLRQ DQG RQH ZDV RQO GD\
 ROG ~~D~~ ~~U~~ ~~W~~ ~~W~~ ~~K~~ ~~H~~ ~~W~~ ~~H~~ ~~V~~ ~~X~~ ~~M~~ ~~H~~ ~~F~~ ~~W~~ ~~V~~ ~~Z~~ ~~H~~ ~~U~~ ~~H~~ ~~H~~ ~~[~~ ~~F~~ ~~O~~ ~~X~~ ~~G~~ ~~H~~ ~~G~~ ~~H~~ ~~U~~ ~~R~~ ~~P~~ ~~F~~ ~~W~~ ~~K~~ ~~H~~ ~~,~~ ~~7~~ ~~V~~ ~~H~~ ~~W~~



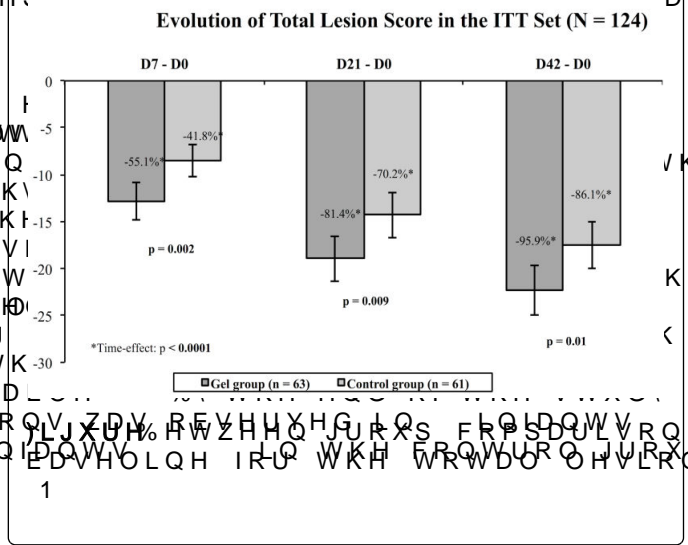
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)RXUWHHQ SDWLHQWV ZHUH H[FOXGHG IURP WKH 33 VHW ,Q WKH JHO JURXS
 LQIDQWV ZHUH ~~Z~~ ~~L~~ ~~W~~ ~~K~~ ~~H~~ ~~G~~ ~~L~~ ~~U~~ ~~D~~ ~~S~~ ~~O~~ ~~U~~ ~~H~~ ~~Q~~ ~~W~~ ~~V~~ ~~G~~ ~~H~~ ~~F~~ ~~L~~ ~~H~~ ~~G~~ ~~H~~ ~~S~~ ~~W~~ ~~R~~ ~~H~~ ~~Q~~ ~~G~~ ~~W~~ ~~K~~ ~~H~~
 WUHDWPHQW DSUHD ~~D~~ ~~P~~ ~~W~~ ~~X~~ ~~W~~ ~~H~~ ~~O~~ ~~P~~ ~~R~~ ~~Q~~ ~~W~~ ~~R~~ ~~I~~ ~~F~~ ~~D~~ ~~U~~ ~~H~~ ~~D~~ ~~Q~~ ~~G~~ ~~R~~ ~~W~~ ~~K~~ ~~H~~ ~~U~~
 LQIDQWV ZHUH H[FOXGHG GXH WR PDMRU ~~Y~~ ~~D~~ ~~S~~ ~~O~~ ~~H~~ ~~P~~ ~~R~~ ~~J~~ ~~B~~ ~~S~~ ~~K~~ ~~L~~ ~~F~~ ~~O~~ ~~D~~ ~~W~~ ~~R~~ ~~Q~~ ~~V~~ ~~D~~ ~~Q~~ ~~G~~ ~~E~~ ~~D~~ ~~V~~ ~~H~~ ~~O~~ ~~D~~ ~~H~~ ~~W~~
 ODVW YLVLW WUHDWPHQW ZLWK DP ~~W~~ ~~K~~ ~~F~~ ~~L~~ ~~O~~ ~~Q~~ ~~W~~ ~~A~~ ~~Q~~ ~~W~~ ~~L~~ ~~R~~ ~~Q~~ ~~K~~ ~~R~~ ~~R~~ ~~S~~ ~~K~~ ~~D~~ ~~W~~ ~~Q~~ ~~H~~ ~~W~~ ~~L~~ ~~V~~ ~~I~~ ~~D~~ ~~Q~~ ~~G~~

FRPSDULVRQV ZHUH SHUIRUPHG XVLQJ WKH IROORZLQJ WHVWV D &KL VTXDUH
 WHVW E 6WXGHQW V 7 WHVW IRU LQGHSHOCHOW YDPSOHV F ALVXHU V HFD FW W

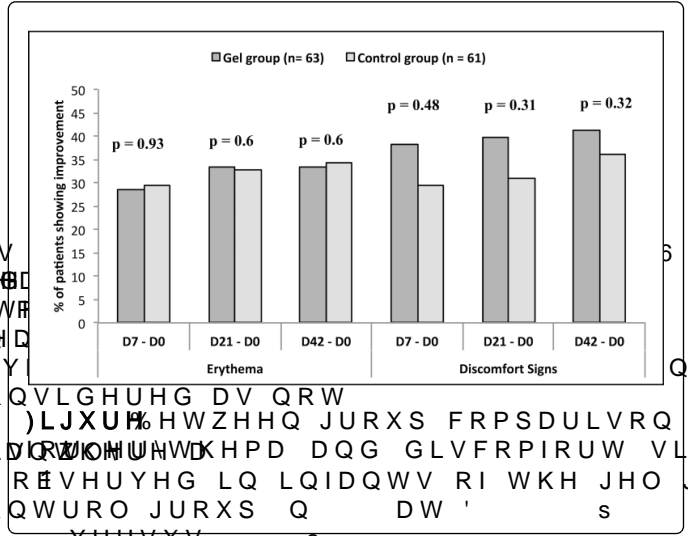
Efficacy

\$ 7/6 GHFUHDVH ZDV REVHUYHG DW
 FRPSDULVRQ ZLWK EDVH LQGLJDUH
 LPSURYHPHQW LQ 7/6 ZDV REVHUYHG LQ
 FRQWURO JURXS (HYFLIXUWKH JHO RYHU K)
 FRQWURO JURXS DW ' H DGOH LQGLJDUH
 GHFUHDVH LQ ERWK JURXS GULQJ
 VWDWLWV QE DRODOW WHU GHFUHDVH LQ WK
 WKH FRQWURO JURXS DW ' DQG ' 7D
 FRPSOHWH UHVROXWLRQ RI WKH OHVLRQV ZDV REVHUYHG LQ
 LQ WKH JHO JURXS FRPSDUHG WR LQIDQWV IRU WKH FRQWURO JURXS VFR



&RPSRQHGW 6' FROHURXS	&RQWURO JURXS DOXH
1	1
*OREDO DIIHFWHG DUHD VFRUH	
"	"
"	"
"	"
*OREDO VFDOH LQWHQVLW\ VFRUH	
"	"
"	"
"	"

\$W ' RQH LQIDQW LQ WKH JHO JURXS
 WKH FRQWURO JURXS SUHVHQWHG ZLWK Z
 DQG VXEMHFW KDG ZRUVHQL
 LQYHVWLJDWRU DQG WKH FRQWURO JURXS
 DV FUHFRYHU\g LQ DQG LQ
 fLPSURYHPHQWg LQ DQG LQ



7DEONKDKQJHV LQ JOREDO FRPSRQHGWV
 EHWZHHQ DVVHVPHQW YLVLWV LQ WKH
 DQG VFDOH LQWHQVLW\ VFRUHV ZHUH
 DUHD DQG LQWHQVLW\ VFRUHV ZHUH
 FRPSDULVRQV IRU FKDKQJHV EHWZHHQ Y
 WKH VWXGHQWV 7 WHVW IRU LQGLJDUH
 5HVROXWLRQV ZHUH GHFUHDVH LQ 7/6 ZDV DOVR
 Q FRPSDUHG WR WKRVH LQ WKH FRQWURO
 YHUVXV s s YHUVXV s

YHUVXV s
 DW WKH HQG RI VWXG\ FRPSOHWH UHFVWLP
 LQ WKH JHO JURXS YHUVXV LQ WKH FRQWURO
 JURXS DW ' DQG ' 7D
 \$ VLPLODU SURSRUWLRQ RI LQIDQWV
 LPSURYHG HU\WKHPD DW ' DQG '
 SURSRUWLRQ RI LQIDQWV LQ WKH JHO
 DW ' DQG ')LJXUH ZLWKRI
 VLJQL}F, DQ ERWK JURXS JOREDO VFRUH
 VLJQV VKRZHGV LQIDQWV DW ' QWV VDWLQJ
 GDWD QRW VKRZQ S

'LVFXVVLRQ
 'HVSLWH SURJUHVV LQ XQGHUVWDQGLQJ
 GHYHORSHPHQW RI 6' QR FRQVHQQXV WUHD

&LWDWBRDQWLQ 3 5LEHW 9 %HFKHU 6% (IILFDF\ DQG 6DIHW3LRM\DLDRSLF BDRSBRPLD WC
3KDVH ,,, &RQWUROOHG 7ULDGR-L&RVPR 7ULFKRO

3DJH RI

GHSHQGWRMLQH SURGXFWLRQ LQ KHDOWK\ &XDMNFWV DRSCH DWR SDE GRHLPD\$WLWLWV 'LDJQ
SDWLHQWV 6NLQ 3KDUPDFRO \$SSO 6NLQ 3K\WHRBUUKHLF GHUPDWLWLWV \$P)DP 3K\VLFLD
&DVDV & 5LEHW 9 \$OYDUH] *HRUJHV 6 6LEDXGLG9(*XDIQRVVR- '6HODODQ 7 <DQ \$.LUF
ORGXODWLRQ RI ,QWHUOHXNLRLQIE\DSG^QHW SSK\CHFRFR FRDQWUROOHG \$lyGBBQGWXSOHWRELV
K\GURWKHUDS\ VQvHSULWRPQW KUGQDPDWRUQRQVWHURLGDO FUHDP IRU WKH WUHDWP
GHUPDWRVHV - (XU \$FDG 'HUPDWRO 9HQHUHRO GHUPDWLWLWV - 'UXJV 'HUPDWRO
OHULDO .& OHQJXDO ; *XHUUHURHyFOLRDXG9D OOHH &QLQDQDQXELR+FKHPLFDO EDVLV RI]
\$Y^QH K\GURWKHUDS\ PHDVXUHG LQ D ODU3K\VERQUMYRI PRUH WKDQ
DWRSLF RU SVRULDWLF SDWLHQWV - (XU \$FDG 'HUPDWRO 9HQHUHRO
OHULDO .LHQ\ & &DVWH[5L]]L 1 6HODV % OHU\ 6 *XHUUHUR '
\$Y^QH WKHUPDO VSULQJ ZDWHU VSGFD)FWLYH FRPSRQHQW ZLWK
SURSHUWLHV - (XU \$FDG 'HUPDWRO 9HQHUHRO