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# **Supplemental Information**

# IncRNA Inc-POP1-1 upregulated by VN1R5 promotes

## cisplatin resistance in head and neck squamous

## cell carcinoma through interaction with MCM5

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## **1** Supplementary Figures





3 Figure S1. Cisplatin-induced resistance in HNSCC and A375/A549 cells. VN1R5

4 expression and cell survival were measured.

1	A. IC <sub>50</sub> values of cisplatin in cisplatin-sensitive and -resistant HN4 cells established								
2	for microarray analysis and subsequent experiments.								
3	B. IC <sub>50</sub> values of cisplatin in cisplatin-sensitive and -resistant HN30 cells established								
4	for microarray analysis and subsequent experiments.								
5	C. IC <sub>50</sub> values of cisplatin in cisplatin-sensitive and -resistant A375 cells established								
6	for microarray analysis.								
7	D. IC <sub>50</sub> values of cisplatin in cisplatin-sensitive and -resistant A549 cells established								
8	for microarray analysis.								
9	E. Microarray analysis of cisplatin-sensitive/-resistant A375 and A549 cells. VN1R5								
10	was upregulated in cisplatin-resistant HNSCC cells.								
11	F. VN1R5 was one of the upregulated proteins in the four cisplatin-resistant cell lines.								
12	G. VN1R5 expression was measured by qPCR and Western blotting in								
13	cisplatin-sensitive and -resistant A375 cells.								
14	H. VN1R5 expression was measured by qPCR and Western blotting in								
15	cisplatin-sensitive and -resistant A549 cells.								
16	** <i>p</i> <0.01, *** <i>p</i> <0.001, **** <i>p</i> <0.0001. Error bars, means ± SDs.								





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3 A. The knockdown efficiency was analyzed by qPCR in HN4/DDP and HN30/DDP



1	B. Procedure of VN1R5 KO in HNSCC cells. HN4/DDP and HN30/DDP stably
2	transfected with sg2- and sg3-targeted vectors were used for further screening and
3	verification. The limited dilution method was used to obtain single cells, after which
4	VN1R5 expression analysis and DNA sequencing were performed.
5	C. After selection of the cell clones grown from single cells, the KO efficiency of
6	VN1R5 was verified by Western blotting.
7	D. After selection of the cell clones grown from single cells, the KO efficiency of
8	VN1R5 was verified by qPCR.
9	E. Compared with NC-transfected cells (black line), HN4/DDP cells with VN1R5
10	downregulation were sensitized to cisplatin (blue line). The $IC_{50}$ values are shown on
11	the right.
12	F. The colony formation ability of KO-VN1R5 HN4/DDP and HN30/DDP cells
13	treated with a specific cisplatin concentration gradient is shown.
14	G. The relative expression levels of VN1R5 in HN4 and HN30 cells stably transduced
15	with LV-VN1R5 were measured by Western blotting.
16	H. The relative expression levels of VN1R5 in HN4 and HN30 cells stably transduced
17	with the VN1R5 lentiviral vector (LV-VN1R5) were measured by qPCR.
18	I. Compared with NC-transfected cells (black line), HN4 cells with VN1R5
19	upregulation (red line) exhibited cisplatin resistance. The $IC_{50}$ values are shown on

J. The colony formation ability of VN1R5-overexpressing HN4 and HN30 cells
 treated with a specific cisplatin concentration gradient is shown.
 K. H&E and Ki-67 staining of xenograft tissues from the KO-VN1R5 and KO-NC
 groups. Scale bar: 100 μm.
 L. H&E and Ki-67 staining of xenograft tissues from the LV-VN1R5 and LV-NC

6 groups. Scale bar: 100 μm.

9

7 \*\* p < 0.01, \*\*\* p < 0.001, \*\*\*\* p < 0.0001. Error bars, means  $\pm$  SDs.



8 (NC, negative control; KO, knockout; LV, lentiviral vector)



A. Microarray analysis to assess the gene expression profiles of KO-VN1R5
 HN4/DDP and HN30/DDP cells.

# B. Microarray analysis to assess the gene expression profiles of VN1R5-overexpressing (LV-VN1R5) HN4 and HN30 cells.

- 5 C. Cell nuclear/cytoplasmic fractionation and qPCR showed the cellular distribution
- 6 of lnc-POP1-1 in HN4 cells. NEAT1, TUG1, MALAT1, U6, BIRC5 and GAPDH
- 7 were used as separation quality standards and endogenous controls, as appropriate.
- 8 D. Cell nuclear/cytoplasmic fractionation and qPCR showed the cellular distribution
- 9 of lnc-POP1-1 in HN30 cells. NEAT1, TUG1, MALAT1, U6, BIRC5 and GAPDH
- 10 were used as separation quality standards and endogenous controls, as appropriate.
- 11 Error bars, means  $\pm$  SDs.

E. FISH analysis of lnc-POP1-1 in HN4 and HN30 cells. (The nuclei were stained
with DAPI. U6 and 18S rRNA were used as nuclear and cytoplasmic markers,
respectively. Scale bar: 10 μm.)





3 A. The relative expression levels of lnc-POP1-1 in HN4/DDP and HN30/DDP cells

- 4 transfected with SS-Inc-POP1-1 were determined by qPCR.
- 5 B. Compared with NC-transfected cells (black line), HN4/DDP cells with lnc-POP1-1
- 6 downregulation were sensitized to cisplatin (blue line). The IC<sub>50</sub> values are shown on



1	C. The colony formation ability of lnc-POP1-1-silenced HN4/DDP and HN30/DDP
2	cells treated with a specific cisplatin concentration gradient is shown.
3	D. The silencing efficiency of ASO-lnc-POP1-1 (ASO-1, ASO-2 and ASO-3) in
4	HN30 and HN30/DDP cells was determined by qPCR.
5	E. H&E and Ki-67 staining of xenograft tissues from the ASO-Inc-POP1-1 and
6	ASO-NC groups. Scale bar: 100 µm.
7	F. The relative expression levels of lnc-POP1-1 in HN4 and HN30 cells stably
8	transduced with the LV-lnc-POP1-1 vector were determined by qPCR.
9	G. Compared with NC-transfected cells (black line), HN4 cells with lnc-POP1-1
10	upregulation were resistant to cisplatin (red line). The IC <sub>50</sub> values are shown on the
11	right.
12	H. The colony formation ability of lnc-POP1-1-overexpressing HN4 and HN30 cells
13	treated with a specific cisplatin concentration gradient is shown.
14	I. H&E and Ki-67 staining of xenograft tissues from the LV-lnc-POP1-1 and LV-NC
15	groups. Scale bar: 100 μm.
16	* $p < 0.05$ , ** $p < 0.01$ , *** $p < 0.001$ , **** $p < 0.0001$ . Error bars, means ± SDs.
17	(NC, negative control; SS, Smart Silencer; LV, lentiviral vector; ASO, antisense
18	oligonucleotide)



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2 Figure S5. VN1R5 and Inc-POP1-1 affect HNSCC cell apoptosis.

- 3 A. Apoptosis was detected using flow cytometry in cisplatin-sensitive/-resistant HN4
- 4 and HN30 cells treated with 0 or 5  $\mu$ M cisplatin for 48 h.
- 5 B. Apoptosis was detected using flow cytometry in HN4/DDP and HN30/DDP cells
- 6 treated with 0 or 10  $\mu$ M cisplatin after KO of VN1R5.
- 7 C. Apoptosis was detected using flow cytometry in HN4/DDP and HN30/DDP cells
- 8 treated with 0 or 10 μM cisplatin after knockdown of lnc-POP1-1.
- 9 D. The expression level of Cleaved Caspase-3 was analyzed by Western blotting in
- 10 cisplatin-sensitive/-resistant HN4 and HN30 cells treated with 5 µM cisplatin for 24 h.

E. The expression level of Cleaved Caspase-3 was analyzed by Western blotting in
 KO-VN1R5 HN4/DDP and HN30/DDP cells treated with 10 μM cisplatin.
 F. The expression level of Cleaved Caspase-3 was analyzed by Western blotting in
 HN4/DDP and HN30/DDP cells treated with 10 μM cisplatin after knockdown of
 Inc-POP1-1.

6 (NC, negative control; SS, Smart Silencer; LV, lentiviral vector; KO, knockout)



8 Figure S6. Inc-POP1-1 was regulated by VN1R5 to affect cisplatin resistance in

9 HNSCC cells.

1	A. Cell viability was detected by CCK-8 assays when lnc-POP1-1 was knocked down
2	in HN4 cells stably transfected with LV-VN1R5. The $IC_{50}$ values are shown on the
3	right.
4	B. Cell viability was detected by CCK-8 assay when lnc-POP1-1 was overexpressed
5	in KO-VN1R5 HN4/DDP cells. The IC <sub>50</sub> values are shown on the right.
6	C, D. Apoptosis was detected using flow cytometry in Inc-POP1-1-overexpressing
7	HN4 and HN30 cells treated with 0 or 5 $\mu$ M cisplatin after KO of VN1R5.
8	E. The expression level of Cleaved Caspase-3 was analyzed by Western blotting in
9	VN1R5-overexpressing HN4 and HN30 cells treated with 5 $\mu$ M cisplatin after
10	knockdown of lnc-POP1-1.
11	F. The expression level of Cleaved Caspase-3 was analyzed by Western blotting in
12	KO-VN1R5 HN4/DDP and HN30/DDP cells treated with 10 $\mu$ M cisplatin after
13	overexpressing lnc-POP1-1.
14	* $p < 0.05$ . Error bars, means $\pm$ SDs.

15 (NC, negative control; SS, Smart Silencer; LV, lentiviral vector; KO, knockout)





3 by VN1R5.



1	B. The common predicted TFs were analyzed with AliBaba2.1 and JASPAR
2	(http://jaspar.genereg.net).
3	C, D. The relative expression levels of Sp1 in cisplatin-sensitive and -resistant
4	HNSCC cells transfected with si-Sp1 were determined by qPCR (C) and Western
5	blotting (D).
6	E, F. The relative expression levels of Sp1 in HN4 and HN30 cells transfected with
7	the Sp1 vector were determined by qPCR (E) and Western blotting (F).
8	G. Sp1 expression were analyzed by Western blotting in HNSCC cells transfected
9	with LV-VN1R5 or KO-VN1R5.
10	H. The relative intensity of p-Sp1 expression in HNSCC cells with VN1R5
11	overexpression or knockout was analyzed.
12	I. Sp1 expression was analyzed by qPCR in HNSCC cells transfected with
13	LV-VN1R5.
14	J. Sp1 expression was analyzed by qPCR in HNSCC cells transfected with
15	KO-VN1R5.
16	K. Compared with NC-transfected cells (black line), HN4/DDP and HN30/DDP cells
17	with Sp1 downregulation were sensitized to cisplatin (blue line).
18	L. 5' serial deletion constructs for the promoter region of the lnc-POP1-1 gene were
19	constructed.
20	M. Relative luciferase activity of different lnc-POP1-1 promoter constructs (5'
21	deletions) in HN4/DDP and HN30/DDP cells cotransfected with si-Sp1 or si-NC.

- 1 \* p < 0.05, \*\* p < 0.01, \*\*\* p < 0.001, \*\*\*\* p < 0.0001. Error bars, means  $\pm$  SDs.
- 2 (NC, negative control; si, siRNA; EV, empty vector; LV, lentiviral vector; KO,



3 knockout; p-Sp1, phosphorylated Sp1)



Figure S8. The promoter activity of Sp1 and the expression of Inc-POP1-1
regulated by VN1R5 were affected by the cAMP/PKA pathway.

7 A. Main pathways and their inhibitors that may affect the promoter activity of Sp1.

8 B. The luciferase activity of the lnc-POP1-1 promoter was measured in
9 cisplatin-resistant HNSCC cells treated with inhibitors (LY294002, SB202190 and
10 H-89 dihydrochloride).

11 C. lnc-POP1-1 expression was analyzed by qPCR in cisplatin-resistant HNSCC cells

12 treated with inhibitors (LY294002, SB202190 and H-89 dihydrochloride).

1	D. The expression levels of phosphorylated Sp1 were analyzed by Western blotting in
2	cisplatin-resistant HNSCC cells treated with a cAMP/PKA pathway inhibitor (H-89
3	dihydrochloride, 2 µM).
4	E. The levels of lnc-POP1-1 and phosphorylated Sp1 were measured in
5	VN1R5-overexpressing HNSCC cells treated with H-89 dihydrochloride (2 $\mu$ M).
6	F. The levels of phosphorylated Sp1 were measured in HN4/DDP and HN30/DDP
7	cells treated with si-PKA by Western blotting.
8	G. The levels of lnc-POP1-1 were measured in HN4/DDP and HN30/DDP cells
9	treated with si-PKA by qPCR.
10	H. The relative expression levels of PKA in HN4 and HN30 cells transfected with
11	PKA-Cα vector (PKA) were determined by Western blotting.
12	I. The levels of lnc-POP1-1 and phosphorylated Sp1 were measured in KO-VN1R5
13	HNSCC cells treated with the PKA vector.
14	* $p < 0.05$ , ** $p < 0.01$ , *** $p < 0.001$ , **** $p < 0.0001$ . Error bars, means $\pm$ SDs.
15	(NC, negative control; si, siRNA; EV, empty vector; LV, lentiviral vector; KO,
16	knockout; p-Sp1, phosphorylated Sp1; H-89, H-89 dihydrochloride; PKA, PKA-Cα)



#### 2 Figure S9. Inc-POP1-1 participated in DNA repair pathways.

3 A. Pathway analysis demonstrated that RBPs of lnc-POP1-1 were involved in several

4 DNA repair pathways in humans.

5 B. γH2AX expression was measured by Western blotting in
6 cisplatin-resistant/cisplatin-sensitive HN4 and HN30 cells.

- 7 C. Representative images of the alkaline comet assays to analyze DNA damage in
- 8 cisplatin-resistant/cisplatin-sensitive HN4 and HN30 cells. Scale bar: 20 μm.

1	D, E. Following exposure to 0 $\mu$ M or 5 $\mu$ M cisplatin for 24 h, the AP sites of
2	cisplatin-resistant/cisplatin-sensitive HN4 (D) and HN30 (E) cells were quantified
3	using an AP site counting kit to analyze DNA damage.
4	F. GO analysis data including the predicted biological processes of RBPs of
5	lnc-POP1-1.
6	G. According to the protein characteristics and predicted binding sites for lnc-POP1-1,
7	5 predicted proteins (PRKDC, MCM5, SUPT16H, KDM2A and UBA52) were
8	selected for subsequent experimental validation.
9	H. RNA pull-down plus Western blot analyses showed that PRKDC, SUPT16H,
10	KDM2A and UBA52 could not be pulled down by lnc-POP1-1 probes in HN4 and
11	HN30 cells transfected with LV-lnc-POP1-1.
12	**** $p < 0.0001$ . Error bars, means $\pm$ SDs.

13 (LV, lentiviral vector)



2 Figure S10. Inc-POP1-1 physically interacted with MCM5 and participated in

### 3 **DNA repair pathways.**

- 4 A. IF analysis of MCM5 in HN4/DDP and HN30/DDP cells. Scale bar: 10 μm.
- 5 B. Pearson correlation analysis of the expression of lnc-POP1-1 and MCM5 in

6 HNSCC tissue. 
$$r^2 = 0.2017$$
, n =70.

- 7 C. The predicted lnc-POP1-1 binding site of MCM5 was obtained from the PRIdictor
- 8 database (http://bclab.inha.ac.kr/pridictor).

1	D. The predicted MCM5-binding sites of lnc-POP1-1 were obtained from the								
2	PRIdictor database (http://bclab.inha.ac.kr/pridictor).								
3	E. Construction of the MCM5-FLAG-Mut vector MCM5(R724)-FLAG, which								
4	mutated CGC to GCC at base pairs 2170 to 2172.								
5	F. The relative expression of MCM5 was detected by Western blotting in HN4 and								
6	HN30 cells transfected with the MCM5-FLAG-WT and MCM5-Mut vectors.								
7	G. The relative expression of MCM5 was detected by qPCR in HN4 and HN30 cells								
8	stably transduced with LV-MCM5.								
9	H. The expression of MCM5 and $\gamma$ H2AX was detected by Western blotting in HN4								
10	and HN30 cells stably transduced with LV-MCM5.								
11	I. Representative images of the alkaline comet assays used to analyze DNA damage in								
12	HN4 and HN30 cells over expressing MCM5. Scale bar: 20 $\mu$ m.								
13	J. Following exposure to 0 $\mu M$ or 5 $\mu M$ cisplatin for 24 h, the AP sites of HN4 and								
14	HN30 cells overexpressing MCM5 were quantified using an AP site counting kit to								
15	analyze DNA damage.								
16	K. Compared with the WT plasmid, the lnc-POP1-1 mutant plasmid endowed HN4								
17	and HN30 cells with sensitivity to cisplatin. The $IC_{50}$ values are shown.								
18	* <i>p</i> <0.05, ** <i>p</i> <0.01, *** <i>p</i> <0.001. Error bars, means ± SDs.								
19	(LV, lentiviral vector; NC, negative control; SS, Smart Silencer; EV, empty vector;								
20	WT, wild-type; Mut, mutation)								



#### 2 Figure S11. MCM5 affected the DNA repair and cisplatin resistance of HNSCC

#### 3 cells by interacting with Inc-POP1-1.

A. Proteins were isolated every 4 h from HN4 and HN30 cells treated with 10 μM
or/and 200 μM CHX for 0-16 h and analyzed by Western blotting.

B. Compared with NC-transfected cells (black line), HN4 cells with MCM5
upregulation exhibited resistance to cisplatin (red line). The IC<sub>50</sub> values are shown on
the right.

9 C. The relative expression of MCM5 was detected by qPCR and Western blotting in

10 HN4/DDP and HN30/DDP cells transfected with si-MCM5.

1	D. Compared with NC-transfected cells (black line), HN4/DDP cells with MCM5
2	downregulation were sensitized to cisplatin (blue line). The $IC_{50}$ values are shown on
3	the right.
4	E. Cell viability was detected by CCK-8 assays when lnc-POP1-1 was knocked down
5	in HN4 cells stably transfected with LV-MCM5. The $IC_{50}$ values are shown on the
6	right.
7	F. Cell viability was detected by CCK-8 assays when lnc-POP1-1 and MCM5 were
8	both knocked down in HN4/DDP cells. The IC50 values are shown on the right.
9	* <i>p</i> <0.05, **** <i>p</i> <0.0001. Error bars, means ± SDs.
10	(NC, negative control; si, siRNA; LV, lentiviral vector; SS, Smart Silencer)

# 1 Supplementary Tables

# **Table S1.** Sequences of qPCR primers.

Prin	iers	Sequences (5'-3')		
VN1D5	Forward	TTCAGTCACAGGTCTAAGTCCA		
VNIKS	Reverse	ACCAAAGAAGTCTAAGGACACCA		
	Forward	CAGAAATCATGAGAGATCATCAGTG		
Inc-POP1-1	Reverse	AAGGAGGTAGATTGGAATCCAGG		
CADDU	Forward	GAACGGGAAGCTCACTGG		
GAPDH	Reverse	GCCTGCTTCACCACCTTCT		
	Forward	CTCGCTTCGGCAGCACATATACT		
Uo	Reverse	ATTTGCGTGTCATCCTTGCGCA		
TUCI	Forward	TCCTTGTTTAGTGCATCTTTGCC		
IUGI	Reverse	TGAGTGGTTATTCTGATAGCCTGC		
	Forward	GCATACGCAGCAGATCAGCAT		
NEALI	Reverse	CCCACAATATAGGCATTTACAAGG		
	Forward	CCTAACCAGGCATAACACAGAAT		
MALAII	Reverse	CGAATGGCTTTGTCTCCGAA		
DIDC5	Forward	GCAATGTCTTAGGAAAGGAGATCA		
BIRC5	Reverse	AGAGAAGCAGCCACTGTTACCA		
G - 1	Forward	GGCAATAACCAGTCCACACCAC		
501	Reverse	GCATTTACCCACACAGCCC		
NACN 45	Forward	TGGACTGACAGCCTCGGTGATG		
MCM5	Reverse	GGATTGCCACACGGTCATCTTCTC		

#### Table S2. Relationship between VN1R5 level and clinicopathologic features (N=83) 1

$\begin{tabular}{ c c c c c } \hline $\mathbf{No.} & $\%$ & $\operatorname{Mean \pm SD}$ & $\operatorname{test value}$ & $P$ Value $$ \\ \hline $\operatorname{Age}$ (years) $$ $ $ $ $ $ $ $ $ $ $ $ $ $ $ $ $ $ $	Chamadanistias	No. of Patients		VN1R5 ΔCt <sup>a</sup>	Non-parametric			
Age (years) $\geq 60$ 38       45.78 $8.960 \pm 1.557$ $< 54.22 Z = 1.549 0.121         Gender       Male       47       56.63 8.718 \pm 1.4798.590 \pm 1.538 Z = 0.505 0.613         Gender       Male       47       56.63 8.718 \pm 1.4798.590 \pm 1.538 Z = 0.505 0.613         Smoking History       Nonsmoker       59 71.08 8.509 \pm 1.497Z = 1.527 Z = 0.505 0.613         Smoking History       Nonsmoker       59 71.08 8.509 \pm 1.497Z = 1.527 Z = 0.505 0.613         Malchohd History       Nondrinker       53 63.86 8.670 \pm 1.534Z = 0.038 0.970         Drinker       30 36.14 8.649 \pm 1.454 Z = 0.038 0.970         Drinker       30 36.14 8.649 \pm 1.454 Z = 0.038 0.970         Starbard       Z = 0.379 0.119 24 28 33.73 8.304 \pm 1.495 Z = 0.379 0.705         Symph Node Metastasis       V = 1.472 Z = 0.379 0.705 0.705 0.119         NM Sage       II-II     $	Characteristics	No.	%	Mean± SD	test value	<i>P</i> value		
$\begin{array}{c c c c c c c } \geq 60 & 38 & 45.78 & 8.960 \pm 1.557 \\ <60 & 45 & 54.22 & 8.411 \pm 1.413 \\ \hline \begin{timesmalineskipped{timesmalineskippedity} \\ \hline timesmalineskippedity \\ \hline \begin{timesmalineskippedity \\ \hline \ebgin{timesmalineskippedity \\ \hline \ \ \ebgin{timesmalineskippedity \\ \hline \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \$	Age (years)							
$<60$ 45 $54.22$ $8.411 \pm 1.413$ $Z=1.549$ $0.121$ Gender         Male         47 $56.63$ $8.718 \pm 1.479$ $Z=0.505$ $0.613$ Female $36$ $43.37$ $8.509 \pm 1.538$ $Z=0.505$ $0.613$ Smoking History         Nonsmoker $59$ $71.08$ $8.509 \pm 1.497$ $Z=1.527$ $0.127$ Alcohol History         24 $28.92$ $9.040 \pm 1.457$ $Z=0.038$ $0.970$ Drinker $53$ $63.86$ $8.670 \pm 1.534$ $Z=0.038$ $0.970$ Drinker $30$ $36.14$ $8.649 \pm 1.454$ $Z=0.038$ $0.970$ Tumor Size(cm) $\leq 4$ $28$ $33.73$ $8.304 \pm 1.460$ $Z=1.560$ $0.119$ Lymph Node Metastas: $pN0$ $51$ $61.45$ $8.592 \pm 1.472$ $Z=0.379$ $0.705$ PNN toge $I$ $41$ $49.40$ $8.500 \pm 1.455$ $Z=0.765$ $0.444$ II-IV $42$ $50.60$ $8.821 \pm 1.537$ $Z=0.765$	≥60	38	45.78	8.960 ± 1.557	7 1 5 4 0	0.121		
Gender         Male         47         56.63 $8.718 \pm 1.479$ Z=0.505         0.613           Female         36         43.37 $8.590 \pm 1.538$ Z=0.505         0.613           Smoking History         Nonsmoker         59 $71.08$ $8.509 \pm 1.497$ Z=1.527         0.127           Smoker         24 $28.92$ $9.040 \pm 1.457$ Z=0.038         0.970           Alcohol History         Nondrinker         53         63.86 $8.670 \pm 1.534$ Z=0.038         0.970           Drinker         53         63.86 $8.670 \pm 1.497$ Z=0.038         0.970           Smokre(cm) $= 55$ 66.27 $8.844 \pm 1.495$ Z=0.038         0.970           Size(cm) $= 28$ $33.73$ $8.304 \pm 1.460$ Z=1.560         0.119           Lymph Node Metastasis $pN0$ 51 $61.45$ $8.592 \pm 1.472$ Z=0.379         0.705           TNM Stage         I-II         41         49.40 $8.500 \pm 1.455$ Z=0.765         0.444           HI-IV         42         50.60 $8.821 \pm 1.537$ Z=0.765         0.444           Moder	<60	45	54.22	8.411 ± 1.413	Z=1.549	0.121		
Male4756.63 $8.718 \pm 1.479$ $8.590 \pm 1.538$ $Z=0.505$ $0.613$ Female36 $43.37$ $8.590 \pm 1.437$ $8.590 \pm 1.538$ $Z=0.505$ $0.613$ Smoking HistoryV $Z=0.505$ $0.613$ Nonsmoker59 $71.08$ $8.509 \pm 1.497$ $24$ $Z=1.527$ $0.127$ Smoker24 $28.92$ $9.040 \pm 1.457$ $Z=1.038$ $0.970$ Alcohol History30 $36.14$ $8.649 \pm 1.454$ $Z=0.038$ $0.970$ Drinker30 $36.14$ $8.649 \pm 1.454$ $Z=0.038$ $0.970$ Tumor Size(cm) $Z=1.560$ $0.119$ $Z=1.560$ $0.119$ $24$ 28 $33.73$ $8.304 \pm 1.460$ $Z=1.560$ $0.119$ $24$ 28 $33.73$ $8.304 \pm 1.460$ $Z=0.379$ $0.705$ $PN0$ 51 $61.45$ $8.592 \pm 1.472$ $S 13.55Z=0.3790.705PNN to pN33238.558.774 \pm 1.553Z=0.7650.444HI-IV4250.608.821 \pm 1.537Z=0.7650.444Pathological DifferentizionZ=0.7650.444Well3744.588.387 \pm 1.4658.855 \pm 1.500Z=1.3790.168Tumor TypeYS.53 \pm 1.436RecurrentZ=1.1600.246Primary6780.728.553 \pm 1.436RecurrentZ=1.1600.246Efficacy of TPF regimeS=0.46 \pm 0.898Z=7.3090.246$	Gender					•		
Female $36$ $43.37$ $8.590 \pm 1.538$ $2=0.303$ $0.613$ Smoking HistoryNonsmoker $59$ $71.08$ $8.509 \pm 1.497$ $Z=1.527$ $0.127$ Smoker $24$ $28.92$ $9.040 \pm 1.457$ $Z=1.527$ $0.127$ Alcohol History $30$ $36.14$ $8.649 \pm 1.457$ $Z=0.038$ $0.970$ Drinker $53$ $63.86$ $8.670 \pm 1.534$ $Z=0.038$ $0.970$ Drinker $30$ $36.14$ $8.649 \pm 1.454$ $Z=0.038$ $0.970$ Tumor Size(cm) $\leq$ $8.844 \pm 1.495$ $Z=1.560$ $0.119$ $\leq 4$ $55$ $66.27$ $8.844 \pm 1.495$ $Z=1.560$ $0.119$ $>4$ $28$ $33.73$ $8.304 \pm 1.460$ $Z=0.379$ $0.705$ Lymph Node Metastas $S92 \pm 1.472$ $Z=0.379$ $0.705$ PN0 $51$ $61.45$ $8.592 \pm 1.472$ $Z=0.765$ $0.444$ III-IV $41$ $49.40$ $8.500 \pm 1.455$ $Z=0.765$ $0.444$ III-IV $42$ $50.60$ $8.821 \pm 1.537$ $Z=0.765$ $0.444$ Pathological Differentation $Z=1.379$ $0.168$ Moderatedly/poorly $46$ $55.42$ $8.885 \pm 1.500$ $Z=1.379$ $0.168$ Tumor Type $Z$ $S.53 \pm 1.436$ $Z=1.160$ $0.246$ Primary $67$ $80.72$ $8.553 \pm 1.436$ $Z=1.160$ $0.246$ Efficacy of TPF regimu $S$ $S.904 \pm 0.898$ $Z-7.309$ $0.008^{**}$	Male	47	56.63	8.718 ± 1.479	7-0.505	0.612		
Smoking History $9$ $71.08$ $8.509 \pm 1.497$ $2 = 1.527$ $0.127$ Smoker24 $28.92$ $9.040 \pm 1.457$ $Z = 1.527$ $0.127$ Alcohol History $30$ $36.14$ $8.670 \pm 1.534$ $8.649 \pm 1.454$ $Z = 0.038$ $0.970$ Drinker $53$ $63.86$ $8.670 \pm 1.534$ $8.649 \pm 1.454$ $Z = 0.038$ $0.970$ Drinker $30$ $36.14$ $8.649 \pm 1.454$ $Z = 0.038$ $0.970$ Tumor Size(cm) $= 2$ $33.73$ $8.304 \pm 1.495$ $Z = 1.560$ $0.119$ $\geq 4$ $28$ $33.73$ $8.304 \pm 1.460$ $Z = 1.560$ $0.119$ Lymph Node Metastas $= 1.472$ $Z = 0.379$ $0.705$ PN0 $51$ $61.45$ $8.592 \pm 1.472$ $2 = 0.379$ $0.705$ PN1 to pN3 $32$ $38.55$ $8.774 \pm 1.553$ $Z = 0.379$ $0.705$ TNM Stage $III-IV$ $42$ $50.60$ $8.821 \pm 1.537$ $Z = 0.765$ $0.444$ III-IV $42$ $50.60$ $8.821 \pm 1.537$ $Z = 0.765$ $0.444$ Pathological Differentation $Z = 0.60$ $Z = 1.379$ $0.168$ Moderatedly/poorly $46$ $55.42$ $8.885 \pm 1.500$ $Z = 1.379$ $0.168$ Tumor Type $Z = 0.765$ $0.246$ $0.246$ Primary $67$ $80.72$ $8.553 \pm 1.436$ $Z = 1.160$ $0.246$ Efficacy of TPF regimu $S = 0.99$ $9.946 \pm 0.898$ $Z = 7.309$ $0.000^{**}$	Female	36	43.37	8.590 ± 1.538	Z=0.303	0.015		
Nonsmoker5971.08 $8.509 \pm 1.497$ $24$ $28.92$ $9.040 \pm 1.457$ $2=1.527$ $0.127$ Alcohol History53 $63.86$ $8.670 \pm 1.534$ $30$ $2=0.038$ $0.970$ Drinker30 $36.14$ $8.649 \pm 1.454$ $2=0.038$ $0.970$ Tumor Size(cm) $\leq 4$ 55 $66.27$ $8.844 \pm 1.495$ $2=1.560$ $2=1.560$ $0.119$ $\leq 4$ 55 $66.27$ $8.844 \pm 1.495$ $2=1.560$ $0.119$ $0.119$ $>4$ 28 $33.73$ $8.304 \pm 1.460$ $2=1.560$ $0.119$ Lymph Node Metastast $51$ $61.45$ $8.592 \pm 1.472$ $8.855$ $2=0.379$ $0.705$ PN051 $61.45$ $8.592 \pm 1.472$ $1.4553$ $2=0.379$ $0.705$ PN1 to pN332 $38.55$ $8.774 \pm 1.553$ $2=0.765$ $0.444$ II-IV42 $50.60$ $8.821 \pm 1.537$ $2=0.765$ $0.444$ Pathological Differention $37$ $44.58$ $8.387 \pm 1.465$ $8.885 \pm 1.500$ $2=1.379$ $0.168$ Moderatedly/poorly46 $55.42$ $8.885 \pm 1.500$ $2=1.379$ $0.168$ Tumor Type $7$ $80.72$ $8.553 \pm 1.436$ $8.119 \pm 1.704$ $2=1.160$ $0.246$ Efficacy of TPF regime $59$ $9.946 \pm 0.898$ $2=7.309$ $0.246$	Smoking History							
Smoker2428.92 $9.040 \pm 1.457$ $Z=1.327$ $0.127$ Alcohol HistoryNondrinker53 $63.86$ $8.670 \pm 1.534$ $Z=0.038$ $0.970$ Drinker30 $36.14$ $8.649 \pm 1.454$ $Z=0.038$ $0.970$ Tumor Size(cm) $\leq 4$ 55 $66.27$ $8.844 \pm 1.495$ $Z=1.560$ $0.119$ $\leq 4$ 28 $33.73$ $8.304 \pm 1.460$ $Z=1.560$ $0.119$ Lymph Node Metastasts $V$ $Z=0.379$ $0.705$ PN051 $61.45$ $8.592 \pm 1.472$ $Z=0.379$ $0.705$ PN1 to pN332 $38.55$ $8.774 \pm 1.553$ $Z=0.379$ $0.705$ TNM Stage $V$ $V$ $V$ $S.500 \pm 1.455$ $Z=0.765$ $0.444$ III-IV42 $50.60$ $8.821 \pm 1.537$ $Z=0.765$ $0.444$ Pathological Differentiation $V$ $S.532 \pm 1.436$ $Z=1.379$ $0.168$ Well37 $44.58$ $8.387 \pm 1.465$ $Z=1.379$ $0.168$ Tumor Type $V$ $S.53 \pm 1.436$ $Z=1.160$ $0.246$ Primary $67$ $80.72$ $8.553 \pm 1.436$ $Z=1.160$ $0.246$ Efficacy of TPF regime $S=0.946 \pm 0.898$ $Z=7.309$ $0.246$	Nonsmoker	59	71.08	8.509 ± 1.497	7 1 507	0.127		
Alcohol History5363.86 $8.670 \pm 1.534$ $8.649 \pm 1.454$ $Z=0.038$ $0.970$ Drinker30 $36.14$ $8.649 \pm 1.454$ $Z=0.038$ $0.970$ Tumor Size(cm) $\leq 4$ 55 $66.27$ $8.844 \pm 1.495$ $>4$ $Z=1.560$ $0.119$ $>4$ 28 $33.73$ $8.304 \pm 1.460$ $Z=1.560$ $0.119$ Lymph Node Metastasis $V$ $V$ $V$ $V$ $V$ pN051 $61.45$ $8.592 \pm 1.472$ $8.774 \pm 1.553$ $Z=0.379$ $0.705$ pN1 to pN332 $38.55$ $8.774 \pm 1.553$ $Z=0.379$ $0.705$ TNM Stage $V$ $V$ $V$ $V$ $V$ $V$ III-IV41 $49.40$ $8.500 \pm 1.455$ $8.821 \pm 1.537$ $Z=0.765$ $0.444$ Pathological Differention $V$ $V$ $V$ $V$ $V$ $V$ Well37 $44.58$ $8.387 \pm 1.465$ $8.885 \pm 1.500$ $Z=1.379$ $0.168$ Tumor Type $V$ $V$ $V$ $V$ $V$ $V$ $V$ Primary $67$ $80.72$ $8.553 \pm 1.436$ $9.119 \pm 1.704$ $Z=1.160$ $0.246$ Efficacy of TPF regime $V$ $V$ $V$ $V$ $V$ $V$ Sensitive $39$ $46.99$ $9.946 \pm 0.898$ $Z = 7.309$ $0.000^{**}$	Smoker	24	28.92	$9.040 \pm 1.457$	Z=1.527	0.127		
Nondrinker53 $63.86$ $8.670 \pm 1.534$ $36.14$ $Z=0.038$ $0.970$ Drinker30 $36.14$ $8.649 \pm 1.454$ $Z=0.038$ $0.970$ Tumor Size(cm) $\leq 4$ 55 $66.27$ $8.844 \pm 1.495$ $28$ $Z=1.560$ $0.119$ $>4$ 28 $33.73$ $8.304 \pm 1.460$ $Z=1.560$ $0.119$ Lymph Node Metastasis $V$ $V$ $V$ $0.705$ pN051 $61.45$ $8.592 \pm 1.472$ $32.$ $Z=0.379$ $0.705$ pN1 to pN332 $38.55$ $8.774 \pm 1.553$ $Z=0.765$ $0.444$ III-IV42 $50.60$ $8.821 \pm 1.537$ $Z=0.765$ $0.444$ III-IV46 $55.42$ $8.885 \pm 1.500$ $Z=1.379$ $0.168$ Moderatedly/poorly46 $55.42$ $8.533 \pm 1.436$ $Z=1.160$ $0.246$ Tumor Type $Z=1.160$ $0.246$ $Z=0.00^{**}$ $Z=0.00^{**}$ Efficacy of TPF regime $Z=0.39$ $Z=0.308$ $Z=0.308$ $Z=0.308$	Alcohol History							
Drinker30 $36.14$ $8.649 \pm 1.454$ $Z=0.038$ $0.970$ Tumor Size(cm) $\leq 4$ $55$ $66.27$ $8.844 \pm 1.495$ $Z=1.560$ $0.119$ >428 $33.73$ $8.304 \pm 1.460$ $Z=1.560$ $0.119$ Lymph Node Metastas $51$ $61.45$ $8.592 \pm 1.472$ $Z=0.379$ $0.705$ pN0 $51$ $61.45$ $8.592 \pm 1.472$ $Z=0.379$ $0.705$ pN1 to pN3 $32$ $38.55$ $8.774 \pm 1.553$ $Z=0.379$ $0.705$ TNM StageIII-IV $42$ $50.60$ $8.821 \pm 1.537$ $Z=0.765$ $0.444$ III-IV $42$ $50.60$ $8.821 \pm 1.537$ $Z=0.765$ $0.444$ Pathological Differention $Well$ $37$ $44.58$ $8.387 \pm 1.465$ $Z=1.379$ $0.168$ Moderatedly/poorly $46$ $55.42$ $8.885 \pm 1.500$ $Z=1.160$ $0.246$ Frimary $67$ $80.72$ $8.553 \pm 1.436$ $Z=1.160$ $0.246$ Efficacy of TPF regimer $I6$ $19.28$ $9.119 \pm 1.704$ $Z=7.309$ $0.246$	Nondrinker	53	63.86	8.670 ± 1.534	7_0.029	0.070		
Tumor Size(cm) $\leq 4$ 5566.27 $8.844 \pm 1.495$ $8.304 \pm 1.460$ $Z=1.560$ $0.119$ >428 $33.73$ $8.304 \pm 1.460$ $Z=1.560$ $0.119$ Lymph Node MetastastpN051 $61.45$ $8.592 \pm 1.472$ $8.774 \pm 1.553$ $Z=0.379$ $0.705$ pN1 to pN332 $38.55$ $8.774 \pm 1.553$ $Z=0.765$ $0.444$ III-IV4149.40 $8.500 \pm 1.455$ $8.821 \pm 1.537$ $Z=0.765$ $0.444$ Pathological Differention46.55.42 $8.885 \pm 1.500$ $Z=1.379$ $0.168$ Moderatedly/poorly46 $55.42$ $8.885 \pm 1.500$ $Z=1.379$ $0.168$ Tumor Type $Primary$ $67$ $80.72$ $8.553 \pm 1.436$ $8.1436$ $Z=1.160$ $0.246$ Efficacy of TPF regime $I6$ $19.28$ $9.119 \pm 1.704$ $Z=7.309$ $0.209^{**}$	Drinker	30	36.14	8.649 ± 1.454	Z=0.038	0.970		
$ \begin{array}{ c c c c c } \leq 4 & 55 & 66.27 & 8.844 \pm 1.495 \\ >4 & 28 & 33.73 & 8.304 \pm 1.460 \end{array} \\ \hline \begin{tabular}{ c c c c c } \leq 55 & 33.73 & 8.304 \pm 1.460 \end{array} \\ \hline \begin{tabular}{ c c c c c } \leq 75 & 33.73 & 8.304 \pm 1.460 \end{array} \\ \hline \begin{tabular}{ c c c c c } Lymph Node Metastasts \\ \hline \begin{tabular}{ c c c c } Lymph Node Metastasts \\ \hline \begin{tabular}{ c c c } PN0 & 51 & 61.45 & 8.592 \pm 1.472 \\ \hline \begin{tabular}{ c c c } PN0 & 51 & 61.45 & 8.592 \pm 1.472 \\ \hline \begin{tabular}{ c c c } PN1 to pN3 & 32 & 38.55 & 8.774 \pm 1.553 \end{array} \\ \hline \begin{tabular}{ c c c } PN1 to pN3 & 32 & 38.55 & 8.774 \pm 1.553 \end{array} \\ \hline \begin{tabular}{ c c } PI1 & 41 & 49.40 & 8.500 \pm 1.455 \\ \hline \begin{tabular}{ c c } II-IV & 42 & 50.60 & 8.821 \pm 1.537 \end{array} \\ \hline \begin{tabular}{ c c } Pathological Differentiation \\ \hline \begin{tabular}{ c c } Pathological Differentiation \\ \hline \begin{tabular}{ c c } Well & 37 & 44.58 & 8.387 \pm 1.465 \\ \hline \begin{tabular}{ c c } S1.455 \\ \hline \begin{tabular}{ c c } Pathological Differentiation \\ \hline \begin{tabular}{ c c } Well & 37 & 44.58 & 8.387 \pm 1.465 \\ \hline \begin{tabular}{ c c } S1.455 \\ \hline \begin{tabular}{ c c } Pathological Differentiation \\ \hline \begin{tabular}{ c c } S1.455 \\ \hline \ \begin{tabular}{ c c } S1.455 \\ \hline \begin{tabular}{ c c } S1.455 \\ \hline \ \begin{tabular}{ c c } S1.455 \\ \hline \ \begin{tabular}{ c c } S2.455 \\ \hline \ \begin{tabular}{ c c } S1.455 \\ \hline \ \begin{tabular}{ c c } S2.455 \\ \hline \ \bedin{tabular}{ c c } S2.455 \\ \hline \ $	Tumor Size(cm)							
>42833.73 $8.304 \pm 1.460$ $Z=1.300$ $0.119$ Lymph Node MetastasispN051 $61.45$ $8.592 \pm 1.472$ $Z=0.379$ $0.705$ pN1 to pN332 $38.55$ $8.774 \pm 1.553$ $Z=0.379$ $0.705$ TNM StageI-II41 $49.40$ $8.500 \pm 1.455$ $Z=0.765$ $0.444$ III-IV42 $50.60$ $8.821 \pm 1.537$ $Z=0.765$ $0.444$ Pathological DifferentitionWell37 $44.58$ $8.387 \pm 1.465$ $Z=1.379$ $0.168$ Moderatedly/poorly46 $55.42$ $8.885 \pm 1.500$ $Z=1.379$ $0.168$ Tumor TypePrimary $67$ $80.72$ $8.553 \pm 1.436$ $Z=1.160$ $0.246$ Efficacy of TPF regimeSensitive39 $46.99$ $9.946 \pm 0.898$ $Z=7.309$ $0.000^{**}$	<u>≤</u> 4	55	66.27	8.844 ± 1.495	7-1 560	0.110		
Lymph Node Metastas:pN05161.45 $8.592 \pm 1.472$ $8.592 \pm 1.472$ $Z=0.379$ 0.705pN1 to pN33238.55 $8.774 \pm 1.553$ $Z=0.379$ 0.705TNM Stage $41$ $49.40$ $8.500 \pm 1.455$ $8.821 \pm 1.537$ $Z=0.765$ 0.444III-IV42 $50.60$ $8.821 \pm 1.537$ $Z=0.765$ 0.444Pathological Different: $8.837 \pm 1.465$ $Z=1.379$ 0.168Moderatedly/poorly46 $55.42$ $8.885 \pm 1.500$ $Z=1.379$ 0.168Tumor Type $8.553 \pm 1.436$ $Z=1.160$ 0.246Primary67 $80.72$ $8.553 \pm 1.436$ $Z=1.160$ 0.246Efficacy of TPF regime $9.946 \pm 0.898$ $Z=7.309$ $0.900^{**}$	>4	28	33.73	$8.304 \pm 1.460$	Ζ=1.300	0.119		
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	Lymph Node Metastas	is						
pN1 to pN332 $38.55$ $8.774 \pm 1.553$ $Z=0.379$ $0.703$ TNM StageI-II4149.40 $8.500 \pm 1.455$ $Z=0.765$ $0.444$ III-IV4250.60 $8.821 \pm 1.537$ $Z=0.765$ $0.444$ Pathological DifferentiationWell3744.58 $8.387 \pm 1.465$ $Z=1.379$ $0.168$ Moderatedly/poorly4655.42 $8.885 \pm 1.500$ $Z=1.379$ $0.168$ Tumor TypePrimary67 $80.72$ $8.553 \pm 1.436$ $Z=1.160$ $0.246$ Efficacy of TPF regimenSensitive39 $46.99$ $9.946 \pm 0.898$ $Z=7.309$ $0.000^{**}$	pN0	51	61.45	$8.592 \pm 1.472$	7-0.270	0.705		
TNM StageI-II4149.40 $8.500 \pm 1.455$ $Z=0.765$ 0.444III-IV4250.60 $8.821 \pm 1.537$ $Z=0.765$ 0.444Pathological Differention3744.58 $8.387 \pm 1.465$ $Z=1.379$ 0.168Well3744.52 $8.885 \pm 1.500$ $Z=1.379$ 0.168Moderatedly/poorly4655.42 $8.885 \pm 1.500$ $Z=1.160$ 0.246Primary67 $80.72$ $8.553 \pm 1.436$ $Z=1.160$ 0.246Recurrent1619.28 $9.119 \pm 1.704$ $Z=1.160$ $0.246$ Efficacy of TPF regimer39 $46.99$ $9.946 \pm 0.898$ $Z=7.309$ $0.00^{**}$	pN1 to pN3	32	38.55	$8.774 \pm 1.553$	$\Sigma = 0.379$	0.703		
I-II4149.40 $8.500 \pm 1.455$ $Z=0.765$ $0.444$ III-IV4250.60 $8.821 \pm 1.537$ $Z=0.765$ $0.444$ Pathological DifferentitionWell3744.58 $8.387 \pm 1.465$ $Z=1.379$ $0.168$ Moderatedly/poorly4655.42 $8.885 \pm 1.500$ $Z=1.379$ $0.168$ Tumor TypePrimary67 $80.72$ $8.553 \pm 1.436$ $Z=1.160$ $0.246$ Efficacy of TPF regimerSensitive39 $46.99$ $9.946 \pm 0.898$ $Z=7.309$ $0.000^{**}$	TNM Stage							
III-IV4250.60 $8.821 \pm 1.537$ $Z=0.703$ $0.444$ Pathological DifferentitionWell3744.58 $8.387 \pm 1.465$ $Z=1.379$ $0.168$ Moderatedly/poorly4655.42 $8.885 \pm 1.500$ $Z=1.379$ $0.168$ Tumor TypePrimary67 $80.72$ $8.553 \pm 1.436$ $Z=1.160$ $0.246$ Recurrent1619.28 $9.119 \pm 1.704$ $Z=1.160$ $0.246$ Efficacy of TPF regimer $Sensitive$ 39 $46.99$ $9.946 \pm 0.898$ $Z=7.309$ $0.000^{**}$	I-II	41	49.40	$8.500 \pm 1.455$	7-0 765	0.444		
Pathological DifferentiationWell3744.58 $8.387 \pm 1.465$ $Z=1.379$ $0.168$ Moderatedly/poorly4655.42 $8.885 \pm 1.500$ $Z=1.379$ $0.168$ Tumor Type $Timor Type$ Primary67 $80.72$ $8.553 \pm 1.436$ $Z=1.160$ $0.246$ Recurrent1619.28 $9.119 \pm 1.704$ $Z=1.160$ $0.246$ Efficacy of TPF regime $Sensitive$ $39$ $46.99$ $9.946 \pm 0.898$ $Z=7.309$ $0.000^{**}$	III-IV	42	50.60	$8.821 \pm 1.537$	Z=0.703	0.444		
Well3744.58 $8.387 \pm 1.465$ Z=1.3790.168Moderatedly/poorly4655.42 $8.885 \pm 1.500$ Z=1.3790.168Tumor TypePrimary67 $80.72$ $8.553 \pm 1.436$ Z=1.1600.246Recurrent1619.28 $9.119 \pm 1.704$ Z=1.1600.246Efficacy of TPF regimeSensitive39 $46.99$ $9.946 \pm 0.898$ $Z=7.309$ $0.000^{**}$	Pathological Different	Pathological Differentiation						
Moderatedly/poorly4655.42 $8.885 \pm 1.500$ $Z=1.379$ $0.108$ Tumor TypePrimary67 $80.72$ $8.553 \pm 1.436$ $Z=1.160$ $0.246$ Recurrent16 $19.28$ $9.119 \pm 1.704$ $Z=1.160$ $0.246$ Efficacy of TPF regimeSensitive39 $46.99$ $9.946 \pm 0.898$ $Z=7.309$ $0.000^{**}$	Well	37	44.58	$8.387 \pm 1.465$	7-1 270	0.168		
Tumor TypePrimary6780.72 $8.553 \pm 1.436$ $Z=1.160$ $0.246$ Recurrent1619.28 $9.119 \pm 1.704$ $Z=1.160$ $0.246$ Efficacy of TPF regimeSensitive39 $46.99$ $9.946 \pm 0.898$ $Z=7.309$ $0.000^{**}$	Moderatedly/poorly	46	55.42	$8.885 \pm 1.500$	Ζ-1.379	0.108		
Primary67 $80.72$ $8.553 \pm 1.436$ Z=1.160 $0.246$ Recurrent1619.28 $9.119 \pm 1.704$ Z=1.160 $0.246$ Efficacy of TPF regimenSensitive39 $46.99$ $9.946 \pm 0.898$ $7-7.309$ $0.000^{**}$	Tumor Type							
Recurrent         16         19.28 $9.119 \pm 1.704$ $Z=1.100$ $0.240$ Efficacy of TPF regimen         Sensitive         39         46.99 $9.946 \pm 0.898$ $Z=7.309$ $0.000^{**}$	Primary	67	80.72	8.553 ± 1.436	7-1 160	0.246		
Efficacy of TPF regimen           Sensitive         39         46.99         9.946 ± 0.898         7-7 309         0.000**	Recurrent	16	19.28	9.119 ± 1.704	Ζ-1.100	0.240		
Sensitive         39         46.99         9.946 ± 0.898         7-7 309         0.000**	Efficacy of TPF regimen							
	Sensitive	39	46.99	$9.946 \pm 0.898$	7 7 200	0.000**		
Resistant         44         53.01         7.524 $\pm$ 0.860         2-7.507         0.000	Resistant	44	53.01	$7.\overline{524 \pm 0.860}$	L-1.309	0.000		

\*\* *p*<0.01

Abbreviations: SD, standard deviation; pN, pathological lymph node status; TNM stage,

tumor-lymph node-metastasis stage. a  $\Delta$ Ct indicates the difference in the cycle number at which a sample's fluorescent signal passes a given threshold above baseline (Ct) derived from a specific gene compared with that of GAPDH in tumor tissues.

## 1 **Table S3.** Relationship between lnc-POP1-1 level and clinicopathologic features

2 (N=83)

Chamataristica	No. of Patients		Lnc-POP1-1 ∆Ct <sup>a</sup>	Non-parametric	Davalua		
Characteristics	No.	%	Mean± SD	test value	P value		
Age (years)							
≥60	38	45.78	$10.586 \pm 1.811$	7_0.261	0.719		
<60	45	54.22	$10.176 \pm 1.665$	Σ=0.301	0.718		
Gender							
Male	47	56.63	$10.273 \pm 1.655$	7_0 671	0.502		
Female	36	43.37	$10.482 \pm 1.852$	$\Sigma = 0.071$	0.302		
Smoking History							
Nonsmoker	59	71.08	$10.364 \pm 1.729$	7_0 222	0.740		
Smoker	24	28.92	$10.361 \pm 1.787$	Z = 0.332	0.740		
Alcohol History							
Nondrinker	53	63.86	$10.254 \pm 1.755$	7_0 711	0.477		
Drinker	30	36.14	$10.558 \pm 1.712$	$\Sigma = 0.711$	0.477		
Tumor Size(cm)							
≤4	55	66.27	$10.491 \pm 1.799$	7_0 722	0.464		
>4	28	33.73	$10.113 \pm 1.604$	Z=0.752	0.404		
Lymph Node Metastas	sis						
pN0	51	61.45	$10.313 \pm 1.846$	7_0.291	0.770		
pN1 to pN3	32	38.55	$10.444 \pm 1.568$	Z-0.201	0.779		
TNM Stage					•		
I-II	41	49.40	$10.175 \pm 1.877$	7-1.070	0.284		
III-IV	42	50.60	$10.548 \pm 1.585$	Z-1.070	0.204		
Pathological Different	Pathological Differentiation						
Well	37	44.58	$10.217 \pm 1.904$	7-0.012	0.362		
Moderatedly/poorly	46	55.42	$10.481 \pm 1.598$	Z=0.912	0.302		
Tumor Type							
Primary	67	80.72	$10.407 \pm 1.779$	7-0.600	0.548		
Recurrent	16	19.28	$10.183 \pm 1.579$	2_0.000	0.346		
Efficacy of TPF regimen							
Sensitive	39	46.99	$11.915 \pm 0.860$	7_7 207	0.000**		
Resistant	44	53.01	$8.\overline{988}\pm0.983$	2-1.201	0.000		

\*\* *p*<0.01

Abbreviations: SD, standard deviation; pN, pathological lymph node status; TNM stage, tumor-lymph node-metastasis stage.

a  $\triangle$ Ct indicates the difference in the cycle number at which a sample's fluorescent signal passes a given threshold above baseline (Ct) derived from a specific gene compared with that of GAPDH in tumor tissues.

1 <b>Table S4.</b> The sequences of Inc-POP1-1 Smart Silence
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Product Name	Sequences (5'-3')
	GCCATGAGTGAGCCACCTT
	CTACAGAAATCATGAGAGA
Inc-POP1-1 Smart	AGTTCCCTCAAGTGTGAAA
Silencer	CAACTGACATCCAACTACAA
	AGCCAAGCTGTCCCTGAATT
	AATCTACCTCCTTCACTGAC

**Table S5.** The sequences of ASO and siRNA.

Product Name	Target Sequences (5'-3')
ASO-Inc-POP1-1 $(1)^*$	CAACTGACATCCAACTACAA
ASO-Inc-POP1-1 (2)	AGCCAAGCTGTCCCTGAATT
ASO-Inc-POP1-1 (3)	AATCTACCTCCTTCACTGAC
si-Sp1	CTCCCAACTTACAGAACCA
si-NF-ĸB	AAAAAAAGGGACTTTCATTGTACTGGT
si-Fos	GGGATAGCCTCTCTTACTA
si-JUN	CCAACATGCTCAGGGAACA
si-TBP	CCTAAAGACCATTGCACTT
si-PKA	ATGTTTGAAAGGATAGTCAAAGC
si-MCM5	GCATCTACTCCATCAAGAA

4 \* The sequence of ASO-Inc-POP1-1 cholesterol-conjugated for *in vivo* ASO delivery.

**Table S6.** VN1R5-CRISPR/cas9-sgRNA target sequences.

NO.	TargetSeq
sgRNA 1	TCTAAGATGATCAAACTTCC
sgRNA 2	GTGACTAATTATCATGTCAA
sgRNA 3	GCAGTATGTGGATGAGAGAC

No.		Sequences (5'-3')
1	Forward	TCTCCTCTTTGATTTCCTCTGCTGC
	Reverse	CACAGTTGGGGTGCAAGGG
2	Forward	TATGCCATACAGAATCAATTTTGGGTG
	Reverse	GTGAAATGATATAGCAGTGAGAGTGAG
3	Forward	CCAGGCTGGAGTGAAGTGG
	Reverse	GATCACCTGAAGTCAGGAGCTCA

# **Table S7.** Sequences of lnc-POP1-1 promoter ChIP primers.

# **Table S8.** Sequences of RIP primers for lnc-POP1-1.

No.		Sequences (5'-3')
P1	Forward	CTGGCCTGTGTGATGAATAGAATATGATGG
	Reverse	GCTGGCTTCCTGCAGAGC
P2	Forward	GGAAGCCAGCTGCCATCC
	Reverse	CTCCCAAGGTGGCTCACTCAT
Р3	Forward	ACCTTGGGAGGGGAACCTC
	Reverse	CAGGGACAGCTTGGCTGG
P4	Forward	CTGTCCCTGAATTCCTGACCTACAGA
	Reverse	CCATGAGCTCCCACCTGCG
P5	Forward	AGCTCATGGCGTGGGAAG
	Reverse	GGAGACTAATCAGCTTTGCCTTGG
P6	Forward	CTGATTAGTCTCCCTGAGCCTCAG
	Reverse	CTCCAATCCTGGTGGCACTGA