Date:April 9 2021
Your Name:Noriko Hirai
Manuscript Title: Cyclin-dependent kinase 4 upregulation mediates acquired resistance of dabrafenib plus trametinib
in BRAF V600E-mutated lung cance_
Manuscript number (if known):

In the interest of transparency, we ask you to disclose all relationships/activities/interests listed below that are related to the content of your manuscript. "Related" means any relation with for-profit or not-for-profit third parties whose interests may be affected by the content of the manuscript. Disclosure represents a commitment to transparency and does not necessarily indicate a bias. If you are in doubt about whether to list a relationship/activity/interest, it is preferable that you do so.

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		Name all entities with whom you have this relationship or indicate none (add rows as needed) Time frame: Since the initial	Specifications/Comments (e.g., if payments were made to you or to your institution) planning of the work
1	All support for the present manuscript (e.g., funding, provision of study materials, medical writing, article processing charges, etc.) No time limit for this item.	_X_None	
		Time frame: past	36 months
2	Grants or contracts from any entity (if not indicated in item #1 above).	_XNone	
3	Royalties or licenses	_XNone	
4	Consulting fees	_XNone	

5	Payment or honoraria for	_ <u>X</u> None	
	lectures, presentations,		
	speakers bureaus,		
	manuscript writing or		
-	educational events Payment for expert	X None	
6	testimony	_ <u>x</u> _none	
	,		
7	Support for attending meetings and/or travel	_XNone	
	g ,		
8	Patents planned, issued or	<u>X</u> None	
	pending		
_			
9	Participation on a Data	XNone	
	Safety Monitoring Board or Advisory Board		
10	Leadership or fiduciary role	X None	
10	in other board, society,	_ <u>X</u> None	
	committee or advocacy		
	group, paid or unpaid		
11	Stock or stock options	_ <u>X</u> None	
12	Receipt of equipment,	<u>X</u> None	
	materials, drugs, medical		
	writing, gifts or other services		
13	Other financial or non-	<u>X</u> None	
	financial interests		
Dia-			fallandar ban
riea	ise summarize the above co	milict of interest in the	tollowing box:

Dr. Hirai has nothing to disclose.		

Date:April 9 2021
Your Name:Yutaka Hatanaka
Manuscript Title: Cyclin-dependent kinase 4 upregulation mediates acquired resistance of dabrafenib plus trametinib
in BRAF V600E-mutated lung cance_
Manuscript number (if known):

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		Time frame: past	36 months
2	Grants or contracts from any entity (if not indicated in item #1 above).	None Sysmex Thermo Fisher Scientific	Grant Grant
3	Royalties or licenses	_XNone	
4	Consulting fees	XNone	

5	Payment or honoraria for	_XNone	
	lectures, presentations,		
	speakers bureaus,		
	manuscript writing or		
	educational events		
6	Payment for expert	_X_None	
	testimony		
7	Support for attending	<u>X</u> None	
	meetings and/or travel		
8	Patents planned, issued or	<u>X</u> _None	
	pending		
9	Participation on a Data	None	
	Safety Monitoring Board or	Novartis Pharma	Lecture's Fee
	Advisory Board	AstraZeneca	Lecture's Fee
10	Leadership or fiduciary role	<u>_X</u> None	
	in other board, society,		
	committee or advocacy		
	group, paid or unpaid		
11	Stock or stock options	_ <u>X</u> None	
12	Receipt of equipment,	<u>X</u> _None	
	materials, drugs, medical		
	writing, gifts or other		
4.5	services		
13	Other financial or non-	<u>_X</u> None	
	financial interests		

Please summarize the above conflict of interest in the following box:

Dr. Hatanaka reports Lecture's Fee from AstraZeneca, from Novartis, grants from Sysmex, grants from Thermo Fisher Scientific, during the conduct of the study; .

Please place an "X" next to the following statement to indicate your agreement:

 $\underline{\textbf{X}} \ \textbf{I certify that I have answered every question and have not altered the wording of any of the questions on this}$

Date:April 9 2021
Your Name: <u>Kanako C Hatanaka</u>
Manuscript Title: Cyclin-dependent kinase 4 upregulation mediates acquired resistance of dabrafenib plus trametinib
in BRAF V600E-mutated lung cance_
Manuscript number (if known):

In the interest of transparency, we ask you to disclose all relationships/activities/interests listed below that are related to the content of your manuscript. "Related" means any relation with for-profit or not-for-profit third parties whose interests may be affected by the content of the manuscript. Disclosure represents a commitment to transparency and does not necessarily indicate a bias. If you are in doubt about whether to list a relationship/activity/interest, it is preferable that you do so.

The following questions apply to the author's relationships/activities/interests as they relate to the <u>current</u> <u>manuscript only</u>.

The author's relationships/activities/interests should be <u>defined broadly</u>. For example, if your manuscript pertains to the epidemiology of hypertension, you should declare all relationships with manufacturers of antihypertensive medication, even if that medication is not mentioned in the manuscript.

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		Time frame: past	36 months
2	Grants or contracts from any entity (if not indicated in item #1 above).	_XNone	
3	Royalties or licenses	_X_None	
4	Consulting fees	_XNone	

5	Payment or honoraria for	_ <u>X</u> None	
	lectures, presentations,		
	speakers bureaus,		
	manuscript writing or		
	educational events		
6	Payment for expert	<u>_X</u> _None	
	testimony		
7	Support for attending	<u>X</u> None	
	meetings and/or travel		
8	Patents planned, issued or	<u>X</u> None	
	pending		
9	Participation on a Data	<u>X</u> None	
	Safety Monitoring Board or		
	Advisory Board		
10	Leadership or fiduciary role	<u>X</u> None	
	in other board, society,		
	committee or advocacy		
	group, paid or unpaid		
11	Stock or stock options	_ <u>X</u> None	
12	Receipt of equipment,	<u>X</u> None	
	materials, drugs, medical		
	writing, gifts or other services		
13	Other financial or non-	X None	
	financial interests		
		•	
Dlas	se summarize the above co	nflict of interest in the fo	ollowing hove

Dr. Hatanaka has nothing to disclose.	

Date:April 9 2021
Your Name:Yuji Uno
Manuscript Title: Cyclin-dependent kinase 4 upregulation mediates acquired resistance of dabrafenib plus trametinib
in BRAF V600E-mutated lung cance_
Manuscript number (if known):

In the interest of transparency, we ask you to disclose all relationships/activities/interests listed below that are related to the content of your manuscript. "Related" means any relation with for-profit or not-for-profit third parties whose interests may be affected by the content of the manuscript. Disclosure represents a commitment to transparency and does not necessarily indicate a bias. If you are in doubt about whether to list a relationship/activity/interest, it is preferable that you do so.

The following questions apply to the author's relationships/activities/interests as they relate to the <u>current</u> <u>manuscript only</u>.

The author's relationships/activities/interests should be <u>defined broadly</u>. For example, if your manuscript pertains to the epidemiology of hypertension, you should declare all relationships with manufacturers of antihypertensive medication, even if that medication is not mentioned in the manuscript.

		Name all entities with whom you have this relationship or indicate none (add rows as needed)	Specifications/Comments (e.g., if payments were made to you or to your institution)
		Time frame: Since the initial	planning of the work
1	All support for the present	_X_None	
	manuscript (e.g., funding,		
	provision of study materials,		
	medical writing, article		
	processing charges, etc.)		
	No time limit for this item.		
		Time frame: past	36 months
2	Grants or contracts from	_XNone	
	any entity (if not indicated		
	in item #1 above).		
3	Royalties or licenses	_XNone	
4	Consulting fees	<u>X</u> None	

5	Payment or honoraria for	_ XNone	
	lectures, presentations,		
	speakers bureaus,		
	manuscript writing or		
	educational events		
6	Payment for expert	_X_None	
	testimony		
7	Support for attending	_XNone	
	meetings and/or travel		
8	Patents planned, issued or	X None	
	pending		
9	Participation on a Data	X None	
	Safety Monitoring Board or		
	Advisory Board		
10	Leadership or fiduciary role	_ XNone	
	in other board, society,		
	committee or advocacy		
	group, paid or unpaid		
11	Stock or stock options	<u>X</u> None	
12	Receipt of equipment,	<u>X</u> None	
	materials, drugs, medical		
	writing, gifts or other		
	services		
13	Other financial or non-	_X _None	
	financial interests		

Please summarize the above conflict of interest in the following box:

Mr. Uno has nothing to disclose.	Mr. Uno has nothing to disclose.			

Please place an "X" next to the following statement to indicate your agreement:

 $\underline{\textbf{X}} \ \textbf{I certify that I have answered every question and have not altered the wording of any of the questions on this}$

Date:April 9 2021
Your Name: Shin-ichi Chiba
Manuscript Title: Cyclin-dependent kinase 4 upregulation mediates acquired resistance of dabrafenib plus trametinib
in BRAF V600E-mutated lung cance_
Manuscript number (if known):

In the interest of transparency, we ask you to disclose all relationships/activities/interests listed below that are related to the content of your manuscript. "Related" means any relation with for-profit or not-for-profit third parties whose interests may be affected by the content of the manuscript. Disclosure represents a commitment to transparency and does not necessarily indicate a bias. If you are in doubt about whether to list a relationship/activity/interest, it is preferable that you do so.

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		Time frame: past	36 months
2	Grants or contracts from any entity (if not indicated in item #1 above).	_XNone	
3	Royalties or licenses	_XNone	
4	Consulting fees	X_None	

5	Payment or honoraria for	X None	
Ū	lectures, presentations,		
	speakers bureaus,		
	manuscript writing or		
	educational events		
6	Payment for expert	_X _None	
	testimony		
7	Support for attending	_XNone	
	meetings and/or travel		
8	Patents planned, issued or	_ XNone	
	pending		
9	Participation on a Data	XNone	
	Safety Monitoring Board or		
	Advisory Board		
10	Leadership or fiduciary role	_ <u>X</u> None	
	in other board, society,		
	committee or advocacy		
	group, paid or unpaid		
11	Stock or stock options	<u>X</u> _None	
10			
12	Receipt of equipment,	_XNone	
	materials, drugs, medical		
	writing, gifts or other services		
13	Other financial or non-	X None	
13	financial interests	_ <u> </u>	
	maneral microsis		

Please summarize the above conflict of interest in the following box:

Mr. Chiba has nothing to disclose.			

Please place an "X" next to the following statement to indicate your agreement:

 $\underline{\textbf{X}} \ \textbf{I certify that I have answered every question and have not altered the wording of any of the questions on this}$

Date:April 9 2021
Your Name: Yasuhiro Umekage
Manuscript Title: Cyclin-dependent kinase 4 upregulation mediates acquired resistance of dabrafenib plus trametinik
in BRAF V600E-mutated lung cance_
Manuscript number (if known):

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		Time frame: past	36 months
2	Grants or contracts from any entity (if not indicated in item #1 above).	_XNone	
3	Royalties or licenses	_X_None	
4	Consulting fees	_XNone	

	T		
5	Payment or honoraria for	_XNone	
	lectures, presentations,		
	speakers bureaus,		
	manuscript writing or		
	educational events		
6	Payment for expert	_ X _None	
	testimony		
7	Support for attending	_XNone	
	meetings and/or travel		
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8	Patents planned, issued or	_ <u>X</u> None	
	pending		
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9	Participation on a Data	XNone	
	Safety Monitoring Board or		
	Advisory Board		
10	Leadership or fiduciary role	_ <u>X</u> None	
	in other board, society,		
	committee or advocacy		
	group, paid or unpaid		
11	Stock or stock options	<u>X</u> None	
12	Receipt of equipment,	<u>X</u> None	
	materials, drugs, medical		
	writing, gifts or other		
	services		
13	Other financial or non-	<u>X</u> None	
	financial interests		

Please summarize the above conflict of interest in the following box:

Dr. Umekage has nothing to disclose.		

Please place an "X" next to the following statement to indicate your agreement:

 $\underline{\textbf{X}} \ \textbf{I certify that I have answered every question and have not altered the wording of any of the questions on this}$

Date:April 9 2021
Your Name: Yoshinori Minami
Manuscript Title: Cyclin-dependent kinase 4 upregulation mediates acquired resistance of dabrafenib plus trametinib
in BRAF V600E-mutated lung cance_
Manuscript number (if known):

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		Time frame: past	36 months
2	Grants or contracts from any entity (if not indicated in item #1 above).	_XNone	
3	Royalties or licenses	_XNone	
4	Consulting fees	_XNone	

5	Payment or honoraria for	_XNone			
	lectures, presentations,				
	speakers bureaus,				
	manuscript writing or				
	educational events	V. NI			
6	Payment for expert	_X_None			
	testimony				
7	Support for attending	X None			
,	meetings and/or travel	_XNone			
	meetings and, or traver				
8	Patents planned, issued or	_XNone			
	pending				
9	Participation on a Data	XNone			
	Safety Monitoring Board or				
	Advisory Board				
10	Leadership or fiduciary role	_XNone			
	in other board, society, committee or advocacy				
	group, paid or unpaid				
11	Stock or stock options	X None			
	Cook of Sook opinons				
12	Receipt of equipment,	_XNone			
	materials, drugs, medical				
	writing, gifts or other				
	services				
13	Other financial or non-	_XNone			
	financial interests				
Dloo	Please summarize the above conflict of interest in the following boy:				

Dr. Minami has nothing to disclose.				

Date:April 9 2021
Your Name: <u>Shunsuke Okumura</u>
Manuscript Title: Cyclin-dependent kinase 4 upregulation mediates acquired resistance of dabrafenib plus trametinib
in BRAF V600E-mutated lung cance_
Manuscript number (if known):

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3	Royalties or licenses	_XNone	
4	Consulting fees	_XNone	

	<u></u>				
5	Payment or honoraria for	_ <u>X</u> None			
	lectures, presentations,				
	speakers bureaus,				
	manuscript writing or				
	educational events				
6	Payment for expert	X None			
	testimony	<u>_x</u> _itolic			
7	Support for attending	<u>X</u> _None			
	meetings and/or travel				
8	Patents planned, issued or	_ <u>X</u> None			
	pending				
9	Participation on a Data	XNone			
	Safety Monitoring Board or				
	Advisory Board				
10	Leadership or fiduciary role	X None			
	in other board, society,				
	committee or advocacy				
	group, paid or unpaid				
11	Stock or stock options	_ <u>X</u> None			
12	Receipt of equipment,	<u>X</u> None			
	materials, drugs, medical				
	writing, gifts or other				
	services				
13	Other financial or non-	_XNone			
	financial interests				
			•		
Dles	Places summarize the above conflict of interest in the following hove				

Dr. Okumura has nothing to disclose.	

Date:April 9 2021
Your Name: Yoshinobu Ohsaki
Manuscript Title: Cyclin-dependent kinase 4 upregulation mediates acquired resistance of dabrafenib plus trametinib
in BRAF V600E-mutated lung cance_
Manuscript number (if known):

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		Time frame: past	36 months
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3	Royalties or licenses	_XNone	
4	Consulting fees	_XNone	

	<u></u>				
5	Payment or honoraria for	_ <u>X</u> None			
	lectures, presentations,				
	speakers bureaus,				
	manuscript writing or				
	educational events				
6	Payment for expert	X None			
	testimony	<u>_x</u> _itolic			
7	Support for attending	<u>X</u> _None			
	meetings and/or travel				
8	Patents planned, issued or	_ <u>X</u> None			
	pending				
9	Participation on a Data	XNone			
	Safety Monitoring Board or				
	Advisory Board				
10	Leadership or fiduciary role	X None			
	in other board, society,				
	committee or advocacy				
	group, paid or unpaid				
11	Stock or stock options	_ <u>X</u> None			
12	Receipt of equipment,	<u>X</u> None			
	materials, drugs, medical				
	writing, gifts or other				
	services				
13	Other financial or non-	_XNone			
	financial interests				
			•		
Dles	Places summarize the above conflict of interest in the following hove				

Dr. Ohsaki has nothing to disclose.	Dr. Ohsaki has nothing to disclose.				

Date:April 9 2021
Your Name:Takaaki Sasaki
Manuscript Title: Cyclin-dependent kinase 4 upregulation mediates acquired resistance of dabrafenib plus trametinib
in BRAF V600E-mutated lung cance_
Manuscript number (if known):

In the interest of transparency, we ask you to disclose all relationships/activities/interests listed below that are related to the content of your manuscript. "Related" means any relation with for-profit or not-for-profit third parties whose interests may be affected by the content of the manuscript. Disclosure represents a commitment to transparency and does not necessarily indicate a bias. If you are in doubt about whether to list a relationship/activity/interest, it is preferable that you do so.

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		Time frame: past	36 months
2	Grants or contracts from any entity (if not indicated in item #1 above).	_XNone	
3	Royalties or licenses	_X_None	
4	Consulting fees	_XNone	

		Ī			
5	Payment or honoraria for	<u>X</u> None			
	lectures, presentations,				
	speakers bureaus,				
	manuscript writing or				
	educational events				
6	Payment for expert	_X _None			
	testimony				
7	Support for attending	<u>X</u> None			
	meetings and/or travel				
8	Patents planned, issued or	_ <u>X</u> None			
	pending				
9	Participation on a Data	_XNone			
	Safety Monitoring Board or				
	Advisory Board				
10	Leadership or fiduciary role	_XNone			
	in other board, society,				
	committee or advocacy				
	group, paid or unpaid				
11	Stock or stock options	_ <u>X</u> None			
12	Receipt of equipment,	<u>_X</u> None			
	materials, drugs, medical				
	writing, gifts or other				
	services				
13	Other financial or non-	_ <u>X</u> None			
	financial interests				
Dlea	Please summarize the above conflict of interest in the following box:				

Dr. Sasaki has nothing to disclose.			