towards high-quality clinical trials and
implementation of genomic medicine

ATLAS Training Program

Course : CRC Training Course

Lecture Title : Supporting participants in cancer clinical trials
(Schedule, compliance, various tests)

Speaker : Mari Takahashi

ATLAS
ASIAN CLINICAL TRIALS NETWORK FOR CANCERS PROJECT

Mari Takahashi

National Cancer Center Hospital Clinical Research Coordinator

■License

- Clinical Laboratory Technologist

■Work Experience

- 2013 – Present (2022) : National Cancer Center Hospital, CRC
- 2001 – 2013 : Private hospital (Clinical Laboratory Technologist)

Supporting Participants In Cancer Clinical Trials

Content of today's presentation

1. Characteristics of patients participating in cancer clinical trials
2. Specific support for patients provided by CRCs
    - Support before administration
    - Support during administration
    - Support after completing administration
3. Summary

1. Characteristics of patients participating in cancer clinical trials

- The participants are patients with cancer
- Adverse drug reactions are unavoidable and varied
- Participants have diverse treatment histories
- Patients face various anxieties and stresses

Supporting Participants In Cancer Clinical Trials

Content of today's presentation

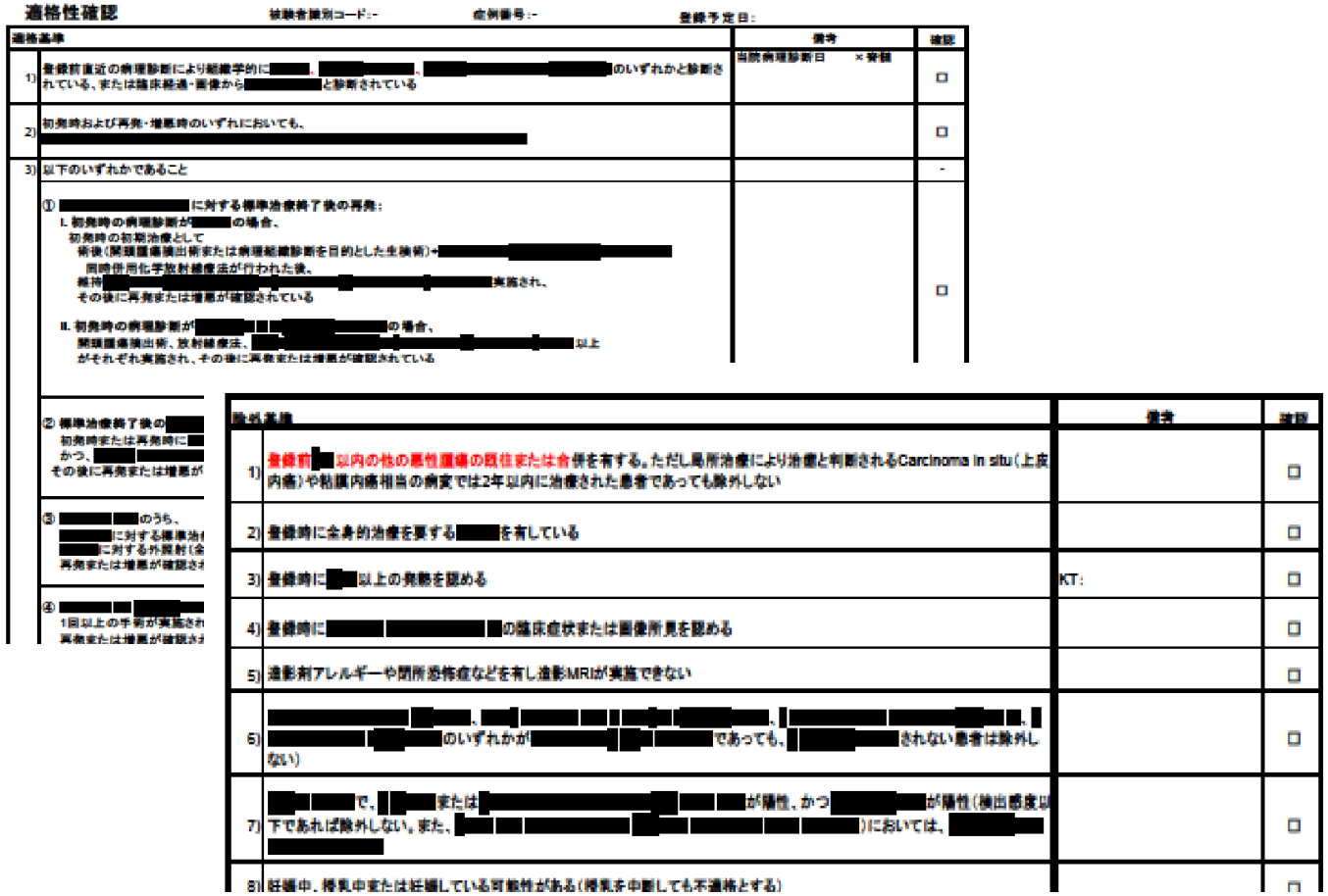
1. Characteristics of patients participating in cancer clinical trials
2. Specific support for patients provided by CRCs
    - Support before administration
    - Support during administration
    - Support after completing administration

2. Specific support for patients provided by CRCs

- Medical chart screening
- Attendance during informed consent
- Supplementary explanation after informed consent
- Support during obtaining consent
- Schedule arrangements from screening tests through the first dose
- Confirmation of eligibility
- Schedule arrangements from the day of the first dose

Medical chart screening

- Collate information against selection / exclusion criteria
- Confirmation of any areas of doubt



適格性確認

適格基準	備考	確認
1) 登録前直近の病理診断により組織学的に[redacted]のいずれかと診断されている、または臨床経過・画像から[redacted]と診断されている	当院病理診断日　×有無	□
2) 初発時および再発・増悪時のいずれにおいても、[redacted]		□
3) 以下のいずれかであること		-
① [redacted]に対する標準治療終了後の再発： i. 初発時の病理診断が[redacted]の場合、 初発時の初期治療として 術後（[redacted]または病理組織診断を目的とした生検術）→[redacted] 同時併用化学放射線療法が行われた後、 維持[redacted]実施され、 その後に再発または増悪が確認されている ii. 初発時の病理診断が[redacted]の場合、 [redacted]以上 がそれぞれ実施され、その後に再発または増悪が確認されている		□
② 標準治療終了後の[redacted] 初発時または再発時に[redacted] かつ、[redacted] その後に再発または増悪が		
③ [redacted]のうち、 [redacted]に対する標準治 [redacted]に対する外照射（全 再発または増悪が確認さ		
④ [redacted] 1回以上の手術が実施され 再発または増悪が確認さ		

除外基準

	備考	確認
1) 登録前[redacted]以内の他の悪性腫瘍の既往または合併を有する。ただし局所治療により治癒と判断されるCarcinoma in situ（上皮内癌）や粘膜内癌相当の病変では2年以内に治療された患者であっても除外しない		□
2) 登録時に全身的治療を要する[redacted]を有している		□
3) 登録時に[redacted]以上の発熱を認める	KT:	□
4) 登録時に[redacted]の臨床症状または画像所見を認める		□
5) 造影剤アレルギーや閉所恐怖症などを有し造影MRIが実施できない		□
6) [redacted]のいずれかが[redacted]であっても、[redacted]きれない患者は除外しない）		□
7) [redacted]で、[redacted]または[redacted]が陽性、かつ[redacted]が陽性（検出感度以下であれば除外しない。また、[redacted]）においては、[redacted]		□
8) 妊娠中、授乳中または妊娠している可能性がある（授乳を中断しても不適格とする）		□

Eligibility criteria confirmation sheet

Attendance during informed consent

- Confirm the content of the doctor’s explanation
- Confirm the patient’s response

Supplementary explanation after informed consent

- Know the patient
- Content and points to be emphasized during the supplementary explanation

Supplementary explanation after informed consent
-Know the patient-

First, confirm the following.

- Patient's personality
- Current medication(s)
- Work situation
- Family structure (who is the key person?)
- Place of residence (as an outpatient)
- Family support system

Supplementary explanation after informed consent

- Content and points to be emphasized during the supplementary explanation -

- Explanation of specific content (frequency of hospital visits, test content, how to take study drug)
- Supplementary explanation regarding adverse drug reactions
- Check level of understanding

Eligibility. Subject schedule_PRTv3.0.xlsx

Schedule (protocol trial) [Cohort A] Subject ID code:×××—×××

case Subject number: ×××—×××

*Please enter the study drug administration date within the red borders. Inputting Day 1 automatically calculates the prescribed study drug administration date and testing dates for each cycle and the associated allowance.

Item	Screening	Course 1 (Day 1)	Course 2 (Day 1)	Course 3 (Day 1)
Prescribed date (automatic calculation)		2021/10/27	2021/10/27	2021/11/17
Study drug administration day allowance (automatic calculation)		(Within registration day +14 days)	11/2 ～ 11/4	11/16 ～ 11/18
Study drug (●●●) administration day				
Study drug administration day allowance (automatic calculation) (assessment before starting from course 2 onward: −2 days)				
Test implementation day				
Consent	◎			
Subject background	◎			
ECOG-PS, KPS	◎		◎	◎
Blood test, biological examination	◎	◎	◎	◎

Protocol number:

[redacted] Medication record

( ) course

Please take after breakfast / after dinner on ( ) month ( ) day.

Your medication per dose is
15 mg (white) ____ tablet, 20 mg (pale red) ____ tablet
Take twice a day (after breakfast, after dinner)

After taking for ■ consecutive days, stop taking the medication for ■ days, then continue to take the medication for a further ■ consecutive days.

If you experience any unusual symptoms, please contact your attending physician at any time.

Please put a check mark next to the item matching the medication status.

Medication date	Date	After breakfast	After dinner
Entry example	9/1	☑ Took medication ☐ Did not take medication	☑ Took medication ☐ Did not take medication
Day 1	/	☐ Took medication ☐ Did not take medication	☐ Took medication ☐ Did not take medication
Day 2	/	☐ Took medication ☐ Did not take medication	☐ Took medication ☐ Did not take medication

Support during obtaining consent

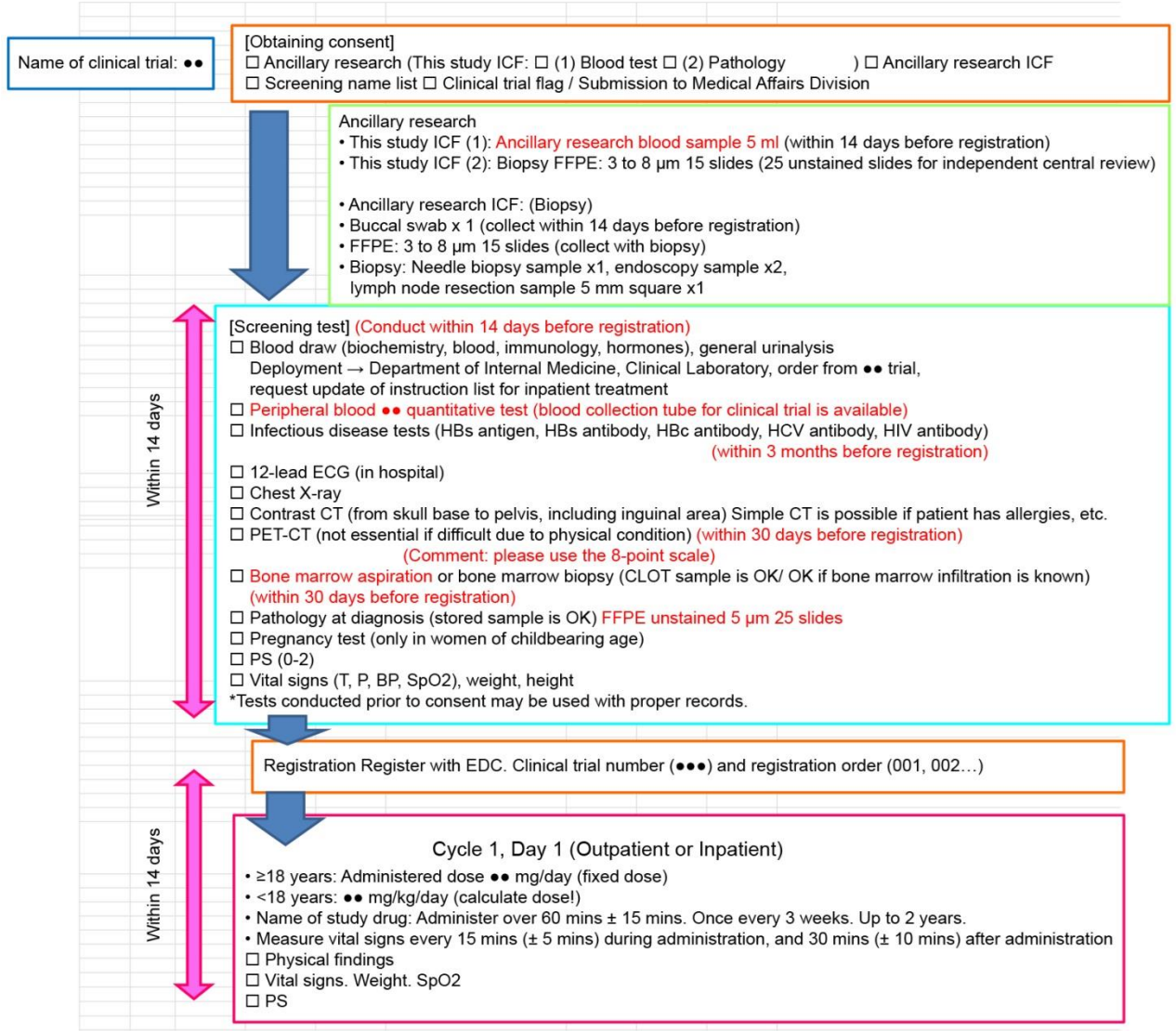
- Are ethical considerations considered?
- Ensuring ethics and reproducibility

#	[Physician-led clinical trial:] Subject ID number:
(S)	
(O)	[Clinical trial explanation] The content was explained by the doctor using the informed consent form, and the CRC provided supplementary explanation. Name of clinical trial: • Informed consent form version: Version 4.0 Optional items: Do not consent • Information explained to: Patient, patient's husband • Time allocated to explanation: Sufficient time was taken to explain the clinical trial • Main questions Question about how to take the study drug • Answer to question: Take one capsule orally per day. No set time or and may be taken with/without food. • Understanding of answer: The patient nodded when hearing the doctor's explanation, and she understood the explanation. • Material provided to patient: Consent form, summary of compensation, clinical trial participation card [Consent to participate in clinical trial] • The subject understands the content of the clinical trial, and written consent to participate in the clinical trial was confirmed with the subject after fully considering participation in the clinical trial.

Schedule arrangements from screening tests to the first dose

Point 1:

- Arrange the schedule with due consideration for the patient and the scheduling status of tests, etc.
- Create management tools



Schedule arrangements from screening tests to the first dose

Point 2:

- Conducting screening tests to align with the first administration date

  Setting the date of the first administration:

  ① Is the patient able to come to the hospital throughout the clinical trial period?

  ② Consider the convenience of the patient, such as work and school.

- Share the schedule with the patient throughout the clinical trial.

Confirmation of eligibility

- Check whether the patient violates the selection criteria or exclusion criteria
- The criteria are checked by several people

被験者識別番号 （ ） [redacted]

※太枠：担当医師記載項目

選択基準 ※治験実施計画書[redacted]版反映

No.	項目	YES	NO
1	病理組織学的に[redacted]がんと診断されている。	☐	☐
2	原発巣および転移巣に対し[redacted]が行われている。	[redacted]	☐
3	総合所見における病期が[redacted]の[redacted]または[redacted]		
4	登録前3か月[redacted]		
5	胸部、腹部、		
6	経口摂取が可		
7	同意取得時年		
8	Eastern Coope		

*2 N1c（UICC TNM分類第8版）も含む（腹膜下層又は腹膜被覆のない結腸もしくは直腸の周囲軟部組織内に腫瘍デポ[redacted]

*3 [redacted]

前化学放射線[redacted]

*4 最新の本邦[redacted]

試験治療とす[redacted]

除外基準 ※治験実施計画書[redacted]版反映

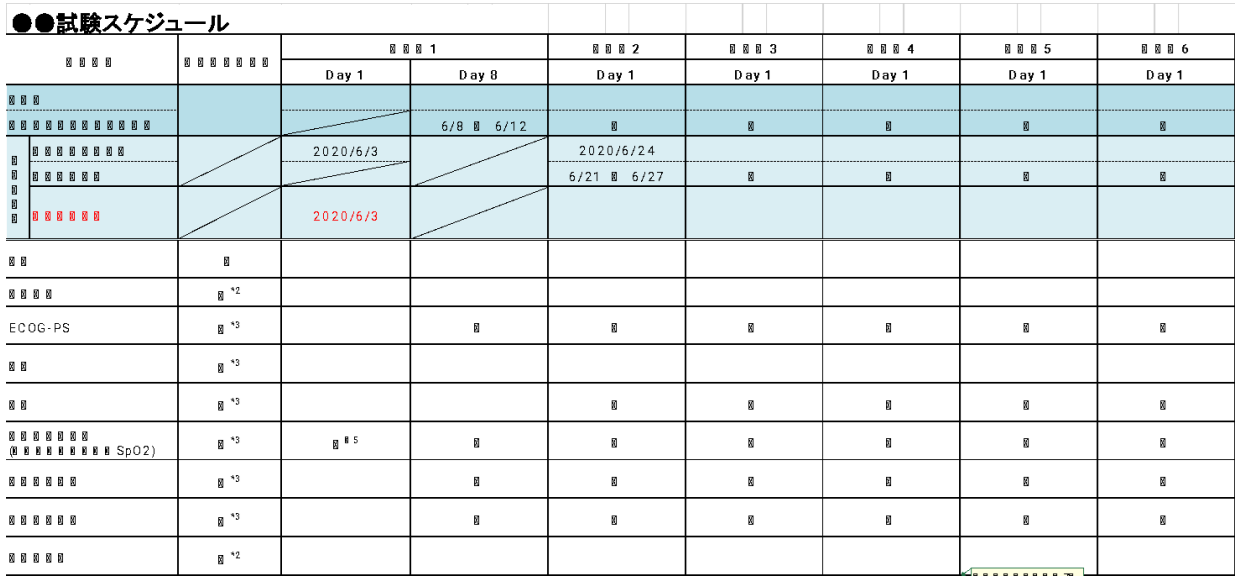
No.	項目	YES	NO
1	[redacted]の治療歴がある。	☐	☐
2	術後補助化学療法*5として[redacted]レジメン以上の治療歴がある（術前化学療法はレジメンとしてカウントしない）。 *5術後補助化学療法の開始時期は規定しない。	☐	☐
3	[redacted]の既往がある*6 *6[redacted]年以上の無再発期間がある患者、又は局所治療により治癒したと判断される皮膚の基底細胞癌又は有棘細胞癌、表在性膀胱癌、子宮頸癌、Carcinoma in situ（上皮内癌）や粘膜内癌相当の病変、全身治療を必要としない非転移性前立腺がんなどを有する患者は登録可能とする。	☐	☐
4	処置を要する局所または全身性の[redacted]を有する。	☐	☐
5	H[redacted]陽性*8 又は[redacted]陽性*9 である。	☐	☐
6	[redacted]陽性である（[redacted]未検でも登録は可能）。	☐	☐
7	コントロール不良の[redacted]を有する。	☐	☐
8	治療を要する[redacted]の既往、またはCT上広範囲にこれらの所見が認められる。	☐	☐
9	重篤な[redacted]*4を有する。	☐	☐

Selection criteria / exclusion criteria checklist

Schedule arrangements from the day of the first dose

- Use various management tools

◎ Overall trial schedule (provided by clinical trial sponsor)



●●試験スケジュール

[redacted]	[redacted]	[redacted] 1		[redacted] 2	[redacted] 3	[redacted] 4	[redacted] 5	[redacted] 6
		Day 1	Day 8	Day 1	Day 1	Day 1	Day 1	Day 1
[redacted]								
[redacted]			6/8 [redacted] 6/12	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]		2020/6/3		2020/6/24				
[redacted]				6/21 [redacted] 6/27	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]		2020/6/3						
[redacted]	[redacted]							
[redacted]	[redacted] *2							
ECOG-PS	[redacted] *3		[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted] *3							
[redacted]	[redacted] *3			[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted] (SpO2)	[redacted] *3	[redacted] *5	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted] *3		[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted] *3		[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted] *2							

◎ Tasks conducted at each visit (created by CRC)

[redacted]

無作為割付

V2(C1D1)
- ☐ EQ-5D-5L・FACT-O （検査実施前に）
- ☐ PS,診察所見(テンプレートphygical examination)
- ☐ 体重(　　kg)、血圧(　　/　　)、脈拍(　　) 体温(　　℃)
- ☐ 採血(血算、Na、K、Ca、Mg、Cr、T-Bil、GGT、ALP、AST、ALT、BUN、TP、Alb、LDH、APTT,INR:必要時)
- ☐ 尿検査(一般)
- ☐ 妊娠検査
- ☐ [redacted]採血
- ☐ [redacted]検査用採血(対象者のみ)
- ☐ PK採血(服用前)採取時間(　:　)
- ☐ AE　併用薬 の確認
- ☐ [redacted]の交付
- ☐ [redacted]研究用血液サンプルの採取(任意同意者)
- ☐ バイオマーカー用サンプルの採取(任意同意者)
- ☐ PK採血(服用1時間後)採取時間(　:　)

V3(C1D8)±3日
- ☐ 採血(血算、Na、K、Ca、Mg、Cr、T-Bil、GGT、ALP、AST、ALT、BUN、TP、Alb、LDH、APTT,INR:必要時)
- ☐ AE　併用薬 の確認

V4(C1D15)±3日
- ☐ 採血(血算、Na、K、Ca、Mg、Cr、T-Bil、GGT、ALP、AST、ALT、BUN、TP、Alb、LDH、APTT,INR:必要時)
- ☐ AE　併用薬 の確認
- ☐ PK採血(服用前)採取時間(　:　)
- ☐ PK採血(服用1時間後)採取時間(　:　)

V5(C1D22)±3日
- ☐ 採血(血算、Na、K、Ca、Mg、Cr、T-Bil、GGT、ALP、AST、ALT、BUN、TP、Alb、LDH、APTT,INR:必要時)

Schedule arrangements from the day of the first dose

◎ **Tests conducted based on a unique schedule (created by a CRC)**

各種スケジュール

◆腫瘍評価 C1D1を起点に1年間は 9週毎(±7日)、その後は12週毎(±7日)に実施。

C1D1	9週後	18週後	27週後	36週後	45週後	54週後
2020/4/20	6/22	8/24	10/26	12/28	3/1	5/3
	6/15	8/17	10/19	12/21	2/22	4/26
	↓	↓	↓	↓	↓	↓
	6/29	8/31	11/2	1/4	3/8	5/10

	66週後	78週後	90週後	102週後	114週後	126週後
	7/26	10/18	1/10	4/4	6/27	9/19
	7/19	10/11	1/3	3/28	6/20	9/12
	↓	↓	↓	↓	↓	↓
	8/2	10/25	1/17	4/11	7/4	9/26

	138週後	150週後	162週後	174週後	186週後	198週後
	12/12	3/6	5/29	8/21	11/13	2/5
	12/5	2/27	5/22	8/14	11/6	1/29
	↓	↓	↓	↓	↓	↓
	12/19	3/13	6/5	8/28	11/20	2/12

◆心エコー 第[redacted]群用：C1D1より16週間毎(±7日)

C1D1	16週後	33週後	48週後	64週後	80週後	96週後
2020/4/20	8/10	11/30	3/22	7/12	11/1	2/21
	8/3	11/23	3/15	7/5	10/25	2/14
	↓	↓	↓	↓	↓	↓
	8/17	12/7	3/29	7/19	11/8	2/28

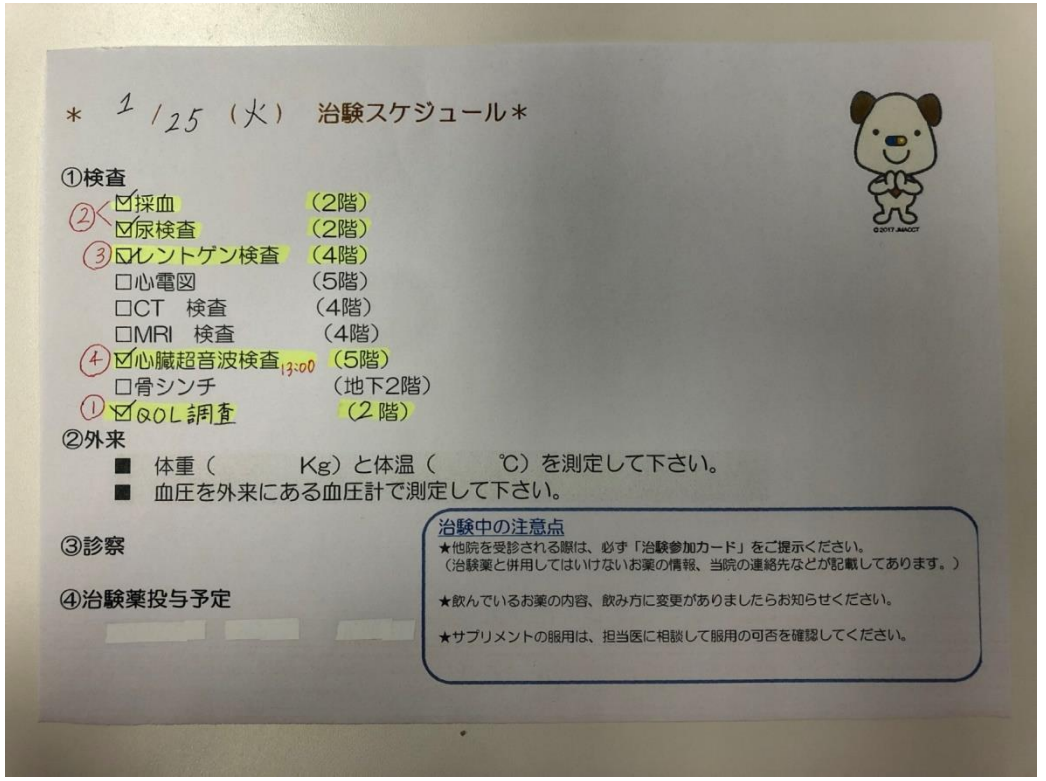
	112週後	128週後	144週後	160週後	176週後	192週後
	6/13	10/3	1/23	5/15	9/4	12/25
	6/6	9/26	1/16	5/8	8/28	12/18
	↓	↓	↓	↓	↓	↓
	6/20	10/10	1/30	5/22	9/11	1/1

◆QOL評価 12週毎(±1週間)に実施。

C1D1	12週後	24週後	36週後	48週後	60週後	72週後	84週後
2020/4/20	7/13	10/5	12/28	3/22	6/14	9/6	11/29
	7/6	9/28	12/21	3/15	6/7	8/30	11/22
	↓	↓	↓	↓	↓	↓	↓
	7/20	10/12	12/28	3/29	6/21	9/13	12/6

	96週後	108週後	120週後	132週後	144週後	156週後	168週後
	2/21	5/15	8/8	10/31	1/23	4/17	7/10
	2/14	5/9	8/1	10/24	1/16	4/10	7/3
	↓	↓	↓	↓	↓	↓	↓

◎ **Memo handed to the patient (created by a CRC)**



＊ 1/25（火） 治験スケジュール＊

①検査
- ②☑採血 （2階）
- ②☑尿検査 （2階）
- ③☑レントゲン検査 （4階）
- ☐心電図 （5階）
- ☐CT 検査 （4階）
- ☐MRI 検査 （4階）
- ④☑心臓超音波検査 13:00 （5階）
- ☐骨シンチ （地下2階）
- ①☑QOL調査 （2階）

②外来
- ■ 体重（ Kg）と体温（ ℃）を測定して下さい。
- ■ 血圧を外来にある血圧計で測定して下さい。

③診察

④治験薬投与予定

治験中の注意点
★他院を受診される際は、必ず「治験参加カード」をご提示ください。
（治験薬と併用してはいけないお薬の情報、当院の連絡先などが記載してあります。）
★飲んでいるお薬の内容、飲み方に変更がありましたらお知らせください。
★サプリメントの服用は、担当医に相談して服用の可否を確認してください。

Supporting Participants In Cancer Clinical Trials

Content of today's presentation

1. Characteristics of patients participating in cancer clinical trials
2. Specific support for patients provided by CRCs
    - Support before administration
    - Support during administration
    - Support after completing administration

2. Specific support for patients provided by CRC -Support during administration-

Confirm implementation of prescribed tests

- Interview with patient
- Management of study drug
- Confirm test results (dosing criteria,dose suspension criteria, dose reduction criteria)
- Report before medical examination

Interviewing patients

Interview location： environment that considers privacy (private room, individual booth)

Interviewing patients

Interview content

- Confirm prescribed tests (vital signs, etc.)
- Adverse events
- Confirm concomitant medication
- Confirm the content of tests and time of medical examination for the next hospital visit

Interviewing patients

Support for early detection of adverse events

- Confirm the contact details, contact method, and available contact times
- Confirm emergency contact details for night-time and holidays
- Specific methods of using the clinical trial participation card
- Suitable timing for contact from the CRC

Interviewing patients

Hints for the conversation…

- Closed and open questions
- Be aware of 5W1H

Study drug management

Prepare a prescription set

For drip infusions : Check dose, administration time, premedication, and post-infusion flush medication.

For oral medication : Check dose, dosing method, relationship with meals, and storage method.

Study drug management

Causes of incorrect dosing

① Causes on the medical personnel side

② Causes on the patient side

③ Causes due to interaction between the patient and medical personnel

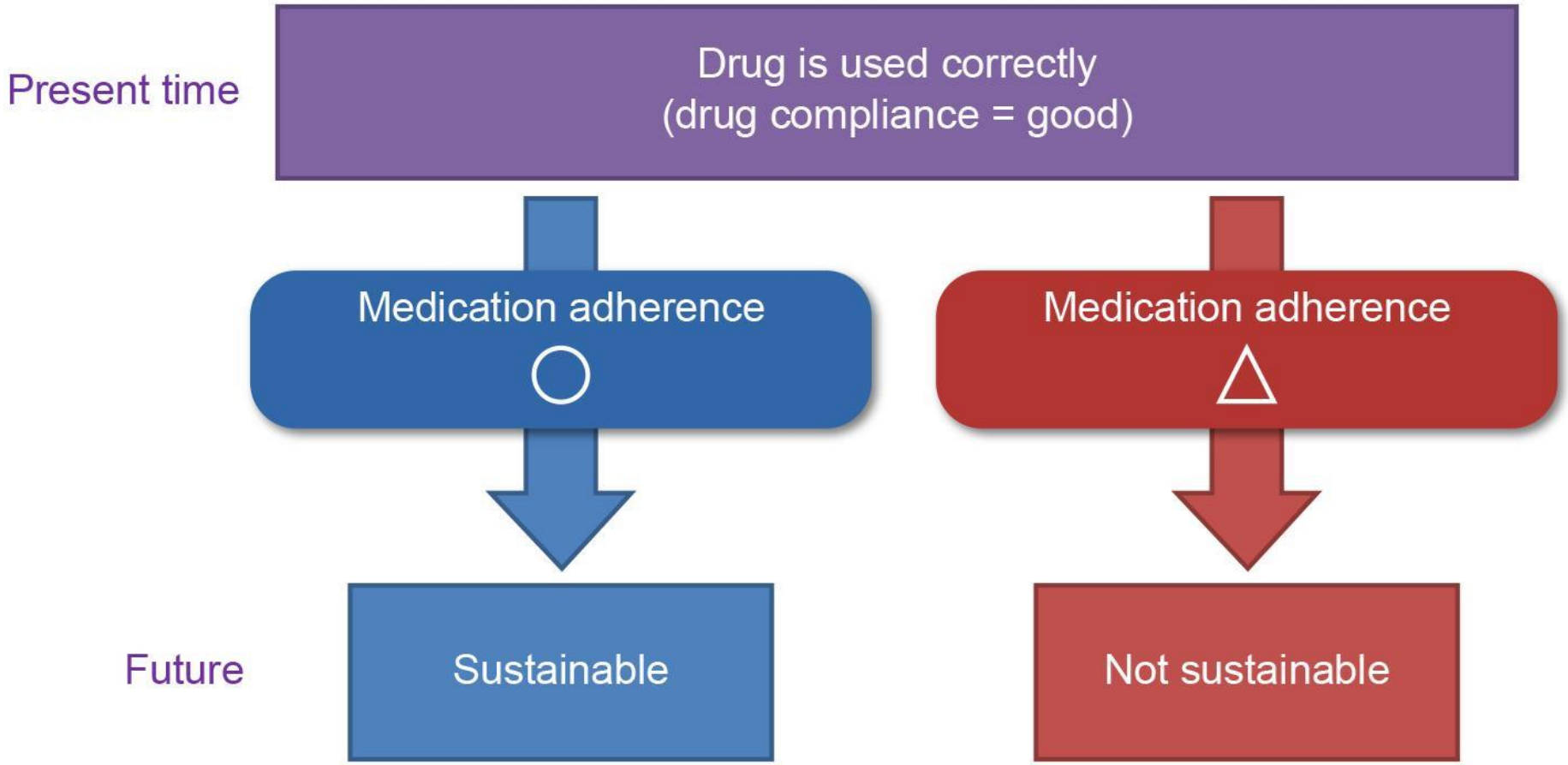
Study drug management

- Efforts to improve compliance/adherence in medical care

Compliance is…
A concept stating that patients receive medical care as instructed by medical professionals

Adherence is…
A concept stating that the patient agrees with the medical care strategy decisions and proactively receives medical care

Study drug management



Source: What is the difference between “Drug compliance” and “Drug adherence”?
~ Assessment of changes in medical awareness and potential risks ~

Supporting Participants In Cancer Clinical Trials

Content of today's presentation

1. Characteristics of patients participating in cancer clinical trials
2. Specific support for patients provided by CRCs
    - Support before administration
    - Support during administration
    - Support after completing administration

2. Specific support for patients provided by CRCs
Support after completing administration

- Support at discontinuing administration
- Follow-up

Support at discontinuing administration

① Schedule arrangements for tests at discontinuation
- Next treatment available ⇒ Support to ensure prompt transition
- Transfer ⇒ When is the last hospital visit?

② Adverse events follow-up, confirm matters that still require strict adherence

③ Hand over to nurses and other departments

④ Psychological support

Follow-up

① Confirm frequency and content

② Confirm survival

3. Summary

To protect the human rights of the patient…

- A space that considers the privacy of the patient
- Environment and atmosphere that makes it easy to converse
- Confirm ethical considerations

To ensure the quality of the clinical trial…

- Prepare and use management tools
- Prepare and systematize study drug prescription sets

To ensure the safety of the patient…

- Communication skills, information-gathering skills
- Improved adherence

References and cited literature

- Yasuo Ohhashi et al., Cancer Clinical Trial Textbook – From Concept to Practice, Igaku-Shoin, 2013, First Edition
- Kazutaka Shimoda et al., CRC Textbook, Igaku-Shoin, 2021, Fourth Edition
- Japanese Society of Pharmaceutical Health Care and Sciences
  https://www.jstage.jst.go.jp/article/jjphcs/38/8/38_522/_pdf
- Practical Manual for Adherence Support
  https://www.erca.go.jp/yobou/zensoku/investigate/pdf/30-2-1_03.pdf
  - What is the difference between “Drug compliance” and “Drug adherence”?
    ～ Assessment of changes in medical awareness and potential risks
    https://www.fizz-di.jp/archives/1061979685.html
  - Concept of Adherence and the Role of the Medical Professional
    ～Considerations from Medication Adherence ～
    https://ogw-media.com/medic/cat_care/1827

Thank you for your kind attention.